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PATHOLOGIC CHANGES IN HUNTINGTON'S CHOREA

WITH SPECIAL REFERENCE TO THE CORPUS STRIATUM *

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NEW YORK

INTRODUCTION

The literature of "chronic progressive chorea," according to Good,[1] dates back to 1842, when Dr. C. O. Waters of Franklin, New York, described in a letter to Dr. Dunglison a peculiar form of chorea, which he said was markedly hereditary, rarely appeared before adult life, was incurable, and always induced dementia. The common people called this disease the "megrims."

Dr. George Huntington,[2] in an article on chorea published in 1872, gave the first good description of the disease which now bears his name; he called it "the hereditary chorea."

Huntington's father and grandfather had both practiced medicine in the eastern end of Long Island for a period conjointly covering seventy-eight years, and had been acquainted with families in which

* This paper, in its present form, was compiled after Dr. Dunlap's death by Dr. Bertram D. Lewin, formerly assistant in neuropathology at the Institute. The first part of the paper, as far as the section headed "Doubtful Cases," was found in the form in which it is printed. It seemed to be practically the form which the author would have considered finished. From this point on, the paper was assembled from notes which, it is almost certain, the author would have considered mere drafts, and would have subjected to careful and critical revision. The editor's work consisted of the arrangement of these parts into the sequence which it seemed would have been the author's sequence. Omissions have been explained in the editor's notes, and one case history with the anatomic observations supplied. Throughout the paper, the editor's notes are included in brackets. We wish to thank Miss Lillian A. Garrett, under whose supervision the technical work was done, and whose intelligent cooperation in the preparation of this paper was indispensable.—George H. Kirby.

1. Good, C. A.: A Review of Chronic Progressive Chorea (Huntington's) with Report of a Case, Am. J. Insan. **57**:21, 1900-1901.

2. Huntington, George: On Chorea, M. & S. Reporter (Philadelphia), January to June, 1872, p. 317.

chorea had existed for generations. Huntington believed that the disease existed almost exclusively on the eastern end of Long Island, where it was confined to a few families. He said that it was hereditary, that it came on gradually, "hardly ever manifesting itself until adult or middle life," that it was incurable, and that it was usually accompanied by insanity and a tendency to suicide. If any member of the family happened to escape the disease, his descendants were free ever afterward.

In 1911, Alzheimer [3] stated that there could hardly be a remaining doubt that in Huntington's chorea severe degenerative processes were regularly present in the cortex of the brain, but that doubt still existed as to whether developmental arrests were also present. Whether the degenerative changes in the cerebral cortex were the anatomic basis for the choreic movements he regarded as doubtful, because of the fact that in various other disease processes, characterized by excessive damage to the cortex, no similar motor disorders or choreic movements are present. Degenerative processes in other parts of the brain and not those in the cerebral cortex were regarded by him as more probably the cause of the motor phenomena in Huntington's chorea.

In three brains that he studied from cases of Huntington's chorea, the most marked changes found anywhere were in the corpus striatum, including both the caudate and the lenticular nuclei. In two of these cases, hardly a nerve cell that could be regarded as still endowed with function was left in these nuclei. Combined with this state of the nerve cells was an enormous increase of small neuroglia nuclei without formation of neuroglia fibers, while lipoid material was excessive in the degenerated nerve cells, neuroglia and vessel walls. In the subthalamic region, the nuclei were also markedly degenerated; they were less degenerated in the optic thalamus, pons and medulla oblongata, although slight degenerative processes were demonstrable even in the spinal cord.

Therefore, Alzheimer believed that one must look on Huntington's chorea as a disease caused by a degenerative process not only in the nerve tissues of the brain cortex, but especially in the corpus striatum and subthalamic region, with slighter involvement of other parts of the central nervous system.

In two cases of chorea that occurred in sepsis and in two cases of rheumatic chorea, he also found changes, especially in the corpus striatum and in the subthalamic region. The changes consisted of small foci of proliferated neuroglia which often were mingled with elements resembling rod cells, and the foci regularly lay in the neighborhood of blood vessels. In the septic cases, he found vascular emboli made up of

3. Alzheimer, A.: Ueber die anatomische Grundlage der Huntingtonschen Chorea und der choreatischen Bewegungen ueberhaupt, Autoreferat., Ztschr. f. d. ges. Neurol. u. Psychiat. **3**:566, 1911.

masses of micrococci, but he did not find bacteria in the rheumatic cases, although the foci were otherwise similar to those in the septic cases. Therefore one might conclude, according to Alzheimer, that septic chorea and rheumatic chorea are associated with embolic foci located especially in the region of the corpus striatum and subthalamic region.

It seemed worth while to bring these statements of Alzheimer to a test in a larger group of cases than he had used. Up to the time of his publication, most authors writing on the anatomic characteristics of Huntington's chorea had reported the basal nuclei as normal, but since then most authors have reported degenerative changes in these parts of the brain, especially in the corpus striatum.

It should be stated at the outset that, in taking up the study of this disease and its relation to the corpus striatum, one encounters a newer and an older set of views regarding the functional importance of this organ.

The newer views are suggested in the preceding summary of Alzheimer's work, which implies—although it does not assert—the association of the striatum with involuntary motor disorders. Other important articles dealing with the newer views on the function of the corpus striatum are especially those of Wilson,[4] on progressive lenticular degeneration, those of C. Vogt,[5] dealing with degenerative changes (called by her état marbré) in the corpus striatum, those of Oppenheim and Vogt on the nature and localization of pseudobulbar paralysis, and articles by various other authors dealing with the histology of the corpus striatum in Huntington's chorea and in paralysis agitans (Jelgersma[6] and Hunt.[7])

The older views are founded on certain observed facts with which one is bound to reckon. These facts deal with focal lesions, mainly softenings, in the corpus striatum and, on the basis of such lesions, evidence has been accumulating for years, and is still accumulating, which tends to show that in man the true function of the corpus striatum is still essentially unknown.

Circumscribed softenings in this organ, usually unilateral but often bilateral, are among the commonest of cerebral lesions. These softenings, when the internal capsule is spared, have so seldom given rise to permanent symptoms of any kind—not to speak of characteristic symp-

4. Wilson, S. A. K.: Progressive Lenticular Degeneration: A Familial Nervous Disease Associated with Cirrhosis of the Liver, Brain **34**:295, 1912.

5. Vogt, Cécilie: Quelques considérations générales à propos du syndrome du corps strié, J. f. Psychol. u. Neurol., Ergänzungshefte, 1911-1912, p. 479.

6. Jelgersma: Neue anat. Befunde bei Paral. agitans u. bei chron. Chorea, Neurol. Centralbl. **27**:995, 1908.

7. Hunt, J. R.: Progressive Atrophy of the Globus Pallidus, Brain **40**:58, 1917.

toms—that a decade ago the region was regarded by the majority of physicians as among the most "silent" and the darkest in pathology of the brain.

Not only have many selective destructive lesions in the human corpus striatum failed to give clear evidence pointing to any definite function for this part, but also recent and careful experimental work, such as that of Wilson [8] on anthropoid animals, in which this body, which is relatively larger than in man, has been first electrically stimulated and then in large part destroyed on one side, has not only failed utterly to establish any clear function for this part, but the animals experimented on differed little if at all from normal controls.

These are well known and undeniable facts of observation; they are not to be set aside simply because other cases have been reported which show clinically tremors, choreiform or athetoid movements coincident with lesions variously observed postmortem (sometimes) in the corpus striatum, (but sometimes also) in the optic thalamus or in the red nucleus or elsewhere. In such cases the clinical symptoms are beyond dispute, and the lesions observed postmortem are likewise beyond dispute, but the interpretation of a necessary dependence of the one on the other, i. e., of the clinical symptoms on the anatomic lesions, is the questionable part. Few if any cases showing these clinical symptoms have been so well studied postmortem as to prove a lesion of the striatum to be the only abnormality present, or to be the sole possible cause that could have produced the symptoms.

PURPOSES OF THE STUDY AND METHODS OF WORK

It was my purpose in undertaking this study, which is based mainly on the anatomic changes found in the brains in seventeen positive cases of Huntington's chorea in the anatomic collection at the Psychiatric Institute, to record mainly the results of my own experience, and to stand as firmly as possible on the ground of demonstrable facts that could be represented for the most part by photographs. Twelve questionable cases of Huntington's chorea were also included in this study, and thirty or more control cases have been used in connection with the choreas.

The study has been especially focussed on the corpus striatum; consequently, the gross and histologic characteristics of this organ are the topics chiefly discussed. No serious attempt will be made at present to interpret the function of this organ on the basis of the observations, unless strong probabilities can be brought out which seem to justify

8. Wilson, S. A. K.: An Experimental Research Into the Anatomy and Physiology of the Corpus Striatum, Brain **36**:427, 1913-1914.

definite views regarding this. Much of the present literature appears to suffer from a surfeit of interpretation on too slight a material basis of fact.

It has seemed best to avoid, for the most part, questions of theory and to make no attempt to present the voluminous literature of this subject since 1911, except to mention the main anatomic observations of others which agree or disagree with the observations in my own material. The present article, therefore, is mainly a record of personal experience gained from a comparative study of the seventeen cases of unquestionable Huntington's chorea, the twelve somewhat doubtful cases and some thirty miscellanous or control cases.

It has seemed best to me not to make a simplified paper by stating a few observed facts and connecting these into a set of conclusions with all the gaps and doubtful places bridged over, but to state to some extent the complexness and the doubts in the situation as they arose, and to indicate the difficulties in which a bias in one direction or another may warp an interpretation into an unjustifiable form. I am convinced that voluminous interpretations are full of danger, especially when studies are incomplete and are not hedged about by abundant safeguards and controls. Facts and half facts are not so difficult to observe, but the danger lies in rushing to conclusions on insufficient and poorly established evidence. Interpretations seem to me to be the most risky of all parts of an investigation. In the complex organs of the central nervous system in which so little of the real working mechanism is actually known or understood, it seems to me of little profit to oneself or to others to study one region in detail and, because it is found to be abnormal, to account for the whole symptomatology of a disease on the basis of that demonstrated abnormality, unless careful study of the rest of the brain shows that no other abnormalities are present which might possibly account for such symptomatology.

In a study such as this, the problem is not so much an interpretation of the function as a determination of the facts concerning a particular region of the brain in Huntington's chorea. This region has lately been brought into the foreground in discussions through many interpretations of its functions as a motor organ in producing involuntary motor disorders.

One of my main objects has been to determine whether or not constant anatomic changes, either gross or microscopic, which were in kind or in location common to all of the brains in true Huntington's chorea, could be found, and if any such constant changes were found, to see whether they were sufficiently characteristic to constitute a so-called pathologic condition of the disorder, or, in other words, to see whether a group of changes could be found in the central nervous system in all cases of Huntington's chorea which would distinguish this disease process from all others.

From this point of view, accidental or concomitant changes were excluded: for example, a hemorrhagic pachymeningitis, which has been recorded among the symptoms of Huntington's chorea. One member in our series of doubtful cases of Huntington's chorea presented a marked example of this. Another positive case in our series showed well marked cerebellar atrophy; a few patients in this positive group had a moderate grade of cerebral arteriosclerosis and one patient had general paralysis, but the series as a whole proved all of the symptoms described to be exceptional.

It has seemed necessary to explain in some detail the methods of work and the principles used in selecting the material for this study, as differences in method and lack of care in selection of material may lead to widely dissimilar results. Doubtless many discrepancies in the literature of Huntington's chorea have come from dissimilarity in material and methods, as well as from differences in point of view.

Sources of personal error will often be referred to. They have been encountered at every stage of this work. Strict accuracy has hardly been attainable anywhere, but at no point has absolute accuracy seemed vital when proper control of one's undividual observations, impressions, reasoning or prejudices could be maintained.

CHARACTER AND SOURCE OF MATERIAL AND SELECTION OF CASES

The character of the material has limited the kind of histologic work that could profitably and safely be done, either in the cortex or in the deep lying structures of the brain. This material, all of which had previously been fixed in formaldehyde, has been sent, together with an abstract of the clinical record, to the Psychiatric Institute through the courtesy of the various state hospitals for the insane in New York State and, at the time of writing, had been accumulating for more than fourteen years. None of the autopsies were done at the institute, and usually the brains were not received until they had been a month or more in formaldehyde. In my experience, formaldehyde injures the stainability of nerve tissues progressively the longer they remain in it, and when this study was begun, I had brains from cases of Huntington's chorea, some of which had been lying in this fixative for periods ranging from a few months to about thirteen years. In the older material the staining reactions were uncertain, and usually were poor.

Moreover, the conditions of initial fixation were largely unknown. Probably in most cases insufficient solution of formaldehyde is used in fixing whole brains; frequently, owing in part to the small size of the containers, only a little more than enough to float the brain is employed. That some brains in this series had been inadequately fixed in too little

solution of formaldehyde was apparent from the fact that it was not a rare experience to find, on sectioning a brain that had been in solution of formaldehyde for weeks, that the basal nuclei and deep parts were still pink, soft and poorly preserved, showing that the formaldehyde had as yet hardly reached those parts.

The corpus striatum—under which term I include the caudate and lenticular nuclei, the latter being subdivided into putamen and globus pallidus—is a deep-lying organ and is among the last parts to be reached by a fixative; consequently, it was often especially poorly preserved. This lack of uniformity in early fixation and preservation, combined with years of soaking in solution of formaldehyde for some brains while others had been soaking only for months, made the tissues of the older and the newer brains too dissimilar to be safely comparable in microscopic details, and it seemed that material thus collected was not suitable for studies of the finer cells. On the other hand, with good control material, it could be used safely for gross study and for study of the general arrangement and distribution of nerve cells, including the number of these; possibly also for study of the presence or absence of increase in neuroglia, and for the study of coarse changes in blood vessels or connective tissues—that is, for a relatively coarse study of structural changes in the nervous system generally, exclusive of finer intracellular changes.[9]

It was found possible, according to this plan, not only to study the brains grossly, but also to study the corpus striatum in the following directions: relative size, consistency and presence or absence of gross focal lesions; presence or absence of nerve cells, their distribution and architectural arrangement, and to some extent the presence and character of the neuroglia content of this organ; also the presence or absence of inflammatory or other changes in the connective tissue and in the blood vessels.

SELECTION OF CASES

It has been considered most important to exclude from the group called true Huntington's chorea every case that was in any way doubtful.

9. I feel less regret in being unable to study the finer details in the nerve cells from the fact that the significance of such changes, except for a few well-recognized types, is often obscure even under the best conditions of preservation and technical procedure. The many unknown factors that may modify nerve cells, including all that vague category included under metabolic changes or dependent on disease processes immediately preceding or leading to death, are so numerous and so little understood in their effects that great caution in interpretation is necessary. It seems much safer to record here only major changes in the cells and especially changes of the nervous system as a whole, changes which cannot raise a doubt as to whether they are transitory in character, or dependent on conditions arising at or near the time of death, or, after death, in the laboratory.

Consequently, the cases diagnosed clinically as Huntington's chorea were divided, according to the family histories and anamneses, into two groups: (1) A so-called positive group, including seventeen cases at the time of writing; every member of this group had, in addition to the characteristic motor disorders and mental symptoms of Huntington's chorea, a family history of uninterrupted heredity from parent to child, and was considered free from all objections. (2) A questionable or doubtful group, including twelve cases, in which unbroken heredity was not proved, though a grandparent or some members of the immediate family may have had the disease. Probably most members of this questionable group had true cases of Huntington's chorea, but in some of them little or no family history of any kind was obtainable. Some were diagnosed as senile chorea.

A third group of about thirty cases, to be used as controls, was picked out from the collection at the institute. These control brains were not ideal for the purpose, as there was practically no normal material; they were chosen more or less at random from such cases as occur in the autopsy service of a hospital for the insane, with some attention to the length of time they had been in solution of formaldehyde in order that they might correspond in this respect to the group of choreas. They were also chosen from various clinical groups such as general paralysis, alcoholic psychoses, arteriosclerosis, senile dementia, paralysis agitans, dementia praecox, etc. They included two cases of electrocution which were reckoned as approximately normal.

METHODS OF EXAMINATION

Gross examinations of the surface and gross examinations after section were made in the brains of all the cases of Huntington's chorea in comparison with the control brains.

In the group of positive cases no constant gross features were noted in the pia mater or in the blood vessels; usually the latter were fairly soft and thin; sometimes they were noted as small. Microscopically also, the blood vessels, though varying somewhat with the age of the patient and from case to case, showed no constant changes, especially no changes of an inflammatory type.

Methods of Estimating Atrophy.—General atrophy of the brain and atrophy of the convolutions, usually a most difficult matter to decide, was estimated in several ways; partly by width of the fissures, size of the convolutions and their firmness or lack of firmness, also by a certain angularity in their course and in their shape as well as by the general appearance of the brain as a whole. I know of no satisfactory way of judging atrophy. It has been represented in part impressionistically as described in the foregoing, but mainly by tables which give the comparative weights of the brains from the cases of Huntington's chorea and of the control brains after section and proper drainage

of the pia mater and ventricles. In general, it may be said that, in the series of seventeen genuine cases, fifteen brains, or approximately 88 per cent, showed a generalized gross atrophy of the cerebral hemispheres — but not of the cerebellum — which was obvious to the eye. Other brains, which did not show plain atrophy, were sometimes described as "swollen looking" so that atrophy, if originally present, may have been masked by swelling, i. e., postmortem swelling.

Methods of Determining Weights.—All of the brains were necessarily weighed and tabulated under the conditions of fixation in formaldehyde, as previously described; the weight at autopsy was frequently not given. Comparative tables of weights of brains from cases of Huntington's chorea and control brains are given further on.

It was found difficult or impossible to determine the true weight of a brain. Some swell and gain considerable weight while in formaldehyde solution; 100 Gm. or more is not an unusual gain of this kind; others remain about the same as at autopsy, or may exceptionally weigh somewhat less. Weights as ordinarily determined at autopsy, owing to differences in fluid retained in the pia arachnoid, ventricles and blood vessels, are also untrustworthy indexes of the real amount of nervous material present. Different weighings of the same brain made at different times never agreed exactly; often the variation was considerable; much depended on a thorough, even drainage of the pia mater, and much care was used in making the conditions in this respect as uniform as possible before weighing any brain. The ventricles in all cases were thoroughly emptied.

The cerebellum, together with the pons and medulla oblongata, was removed by a cut passing as nearly as possible from the anterior border of the pons to the exits of the fourth nerve roots; after suitable drainage, this part was weighed. The cerebral hemispheres were separated in the median line, and each hemisphere was then sectioned either in a semihorizontal direction, as described below, or in a transverse direction. Each cerebral hemisphere was weighed separately, after having been well drained in damp towels to about the same degree of dryness. The parts of the brain were then reassembled and weighed as a whole.

If sections for embedding had been removed from any part of a brain before it was weighed, the loss from this cause was estimated and was added to the weight as shown by the scales. Such estimated losses were tested for accuracy either by weighing a similar amount of tissue cut for this purpose from a control brain, by first estimating the weight of the material cut out for embedding from certain brains and afterward testing the correctness of this estimate by weighing this material. With such checks, sufficiently accurate estimates could be made; it was seldom that more than 15 or 20 Gm. had been removed from a brain in any case, and I feel that the weights, as given in the accompanying tables, can be trusted as fair.

Corpus Striatum.—The corpus striatum was examined grossly as follows: In all of the brains, after the consistency and general appearance of this organ at the levels of section were noted, the greatest transverse width of the lenticular nucleus as a whole was measured in millimeters as was the width of its external subdivision, the putamen; the greatest length of the lenticular nucleus was also measured, and the results of all these measurements were tabulated. The aim was to have the plane of the first semihorizontal section split the anterior commissure, on the mesial aspect of the hemisphere, and pass out laterally through the horizontal part of the fissure of Sylvius, coinciding both

in direction and in level with this part of the fissure. This cut is transverse to the brain stem, and it lays open the corpus striatum in a uniform way nearly, but not quite, at its greatest width. It is of course impossible to make every cut strike the landmarks in exactly the same way, especially when distortion or laceration of the brain is present, but errors from this source are slight and probably balance one another when a large number of cases is examined.

When the cerebral hemispheres were cut transversely, the section passed through the anterior part of the foramen of Monro. Measurements of the corpus striatum were also made at the levels of these transverse cuts but were not tabulated.

The horizontal and the transverse levels, used for measurements of the striatum and its parts, may be seen in plate 2, which represents the size and gross appearances of this organ both in Huntington's chorea and in the control cases. An asymmetry of the corpora striata was not noted on the two sides in any case of Huntington's chorea.

REGIONS STUDIED AND STAINS USED

A liberal number of slices for embedding were taken from the corpus striatum and the optic thalamus at the horizontal and transverse levels described, so that the regions examined in the cases of chorea and in the control cases were similar and comparable. Sections of the red nucleus were also regularly taken throughout the series and, in certain cases, sections from the corpus Luysii and from the dentate nucleus of the cerebellum. Sections were also taken from various cortical areas in all cases, including several from different parts of the frontal lobes, at least one from the upper end of the central convolutions, from the parietal lobes, from the external aspect of the temporal lobes, and from the cornu ammonis; also from the occipital lobes, the cerebellum, the medulla oblongata, and the spinal cord, when this was available.

Among the stains employed, the most useful were toluidin blue, hematoxylin and eosin, van Gieson's stain, Sims' hematoxylin stain, Weigert's neuroglia stain, and Weigert's myelin sheath stain as modified by Wolters and myself. Occasionally, frozen sections were used for Cajal's corrosive sublimate-gold chloride neuroglia method, for the Bielschowsky nitrate of silver method, for Scharlach R, and for the iron hematoxylin methods.

NERVE CELLS IN THE CORPUS STRIATUM

In order to arrive at concrete results regarding the state of the nerve tissues of the corpus striatum, it was desirable to know, in every case, the average number of nerve cells present per microscopic field in the various subdivisions of this organ. Accordingly, in the caudate nucleus, in the putamen, and in the globus pallidus nerve cells were actually counted, case by case and field by field, in the whole series of cases. The microscopic fields counted were all of the same size; the sections

examined, with rare exceptions, were all 8 microns in thickness; consequently, with the few exceptions mentioned, the same amount of nerve tissue was examined in each microscopic field.

The method of counting for the putamen may be illustrated as follows: All the nerve cells in perhaps twenty or more microscopic fields, situated in different parts of the anterior third of this nucleus, would be counted; the figures obtained in each microscopic field would be set down in a column and added together; the sum thus obtained, divided by the number of fields counted, would give the average number of nerve cells per microscopic field in the anterior third of the putamen. Other regions in this nucleus and in other parts of the corpus striatum would be counted in the same way. In counting, no attempt was made to differentiate between the varieties of nerve cells present. Merely the number of such cells was sought.

The numerals thus obtained, which showed the average number of nerve cells in any particular region, were written down in a diagrammatic sketch of the corpus striatum; such a sketch was prepared for every patient examined; the numerals were put down in that part of the diagram in which the counts had actually been made. By means of such diagrams one could see at a glance, in any of the cases, what number of nerve cells had been found in any part of the corpus striatum, and could thus compare case with case. A table of such diagrams grouped according to diagnosis is given in plate 4.

No attempt was made to reckon the number of nerve cells present in a standard amount of nerve tissue, such as a cubic millimeter. The problem was to determine, not the absolute number of nerve cells in a given mass of tissue, but whether the average content of nerve cells of a microscopic field in the corpus striatum in Huntington's chorea differed numerically in any essential way from an average microscopic field of the same size in the corpus striatum of other cases of insanity, or whether it differed from normal cases.

To avoid errors in counting, errors which might arise from personal bias or other reasons, the mounted sections were mixed and were given to me, with the labels covered, by a second person who kept a record of the sections examined and of the counts. I did not know what cells I had counted until days afterward. Besides this, several other members of the institute personnel who knew nerve cells but who had no inkling of the problem also counted the cells; so that in every case the counting was done by more than one person and most of the cells were counted by four people at least. It is not easy, even for the same individual, to count exactly the same number of nerve cells twice in the same field, but variations were not large and I feel that the counts, while they may be faulty in some of the cases in which nerve cells stained poorly and were hard to recognize, represent a close approximation to the true state of things. The existence of minor errors, however, cannot in the least obscure or invalidate the main positive results brought out in the table of diagrams (plate 4).

Sections were cut uniformly at 8 microns for counting purposes; all the microscopes used were standardized for the size of the field by the use of a Zeiss stage micrometer. For convenience in counting, the field was subdivided into quadrants by fine strands of silk placed crosswise in the eye piece. This subdivision was small enough to make counting easy as, in a normal putamen, only about fifteen or twenty nerve cells would be found in a single quadrant.

The nerve cells of the globus pallidus were counted without regard to varieties, all cells that could be seen plainly with the low power of the micro-

Explanation of Plate 1

Plate 1.—An attempt to show by diagrams the situation, and to some extent the intensity, of several disease processes affecting the corpus striatum. The upper square indicates the chief anatomic regions under discussion, with some of their connections. In the other four squares, the position of the cross hatching in the diagrams indicates the position of the disease process represented, and the depth of the cross hatching is intended to indicate the intensity of the process. A question mark means that the region may be abnormal, but that this is uncertain or needs confirmation.

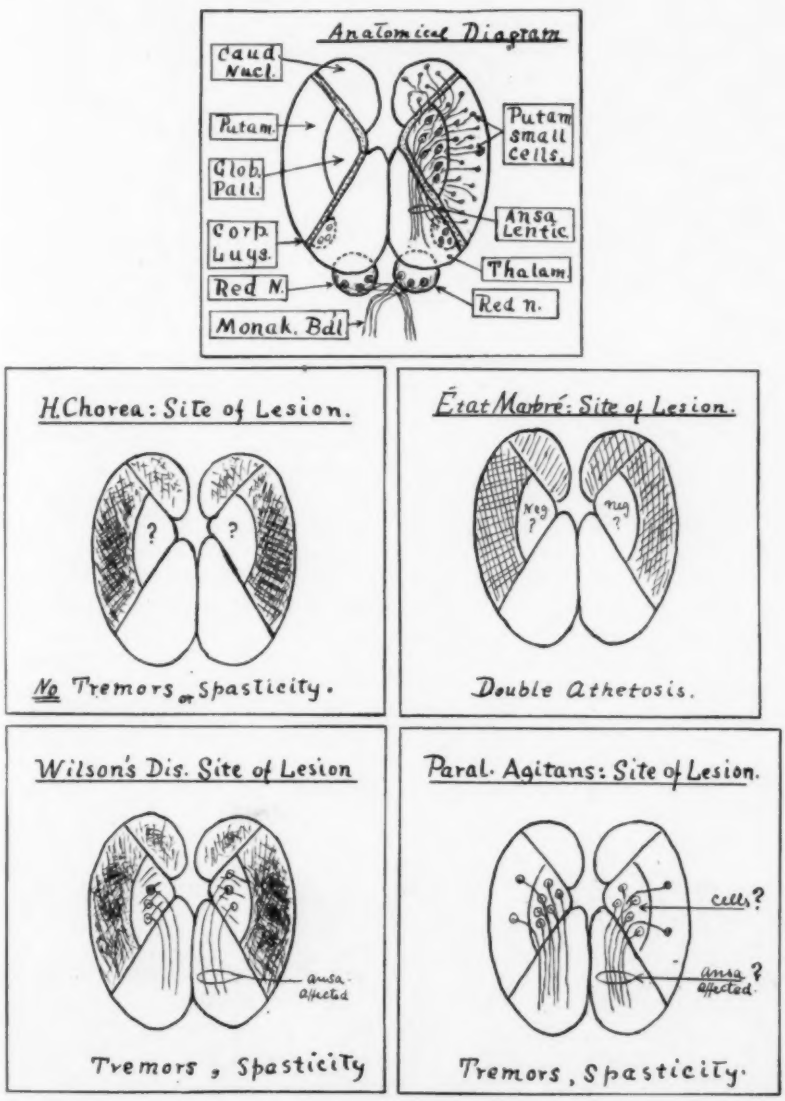
For example, in the square assigned to Huntington's chorea, the cross hatching indicates that the pathologic changes are least in the caudate nucleus and greatest in the middle and posterior parts of the putamen. The globus pallidus, which is greatly reduced in size, may be affected also, but the cell counts and examinations of the nerve fibers indicated that its small size was probably secondary to loss of nerve elements normally entering it from without, i. e., from the putamen and caudate nucleus, and that its nerve cell outfit and the ansa lenticularis were probably intact. This, however, is a difficult point to decide and needs further confirmation; hence the question mark.

In Wilson's disease, as schematized, the cross hatching indicates that the main stress of the process likewise falls on the same areas as in Huntington's chorea, but the more intense focal hatchings mean that actual focal lesions, with loss of substance and formation of cavities, occurred in some of Wilson's cases, though these foci were not necessary accompaniments and were not present in all of the cases. Wilson makes the statement that in three of his cases the globus pallidus was affected, though the main focus of disease was in the putamen, and that in two cases the ansa lenticularis was affected. In the other ten cases reported in his article, the ansa was not examined.

Madame Vogt's reports on her cases of état marbré of the corpus striatum justify about the schema given. Her limitation in the text of the pathologic condition to the caudate nucleus and the putamen agrees with her illustrations as far as état marbré is concerned, but the illustrations also show a globus pallidus greatly reduced in volume, fully as much so as in Huntington's chorea. She fails to list this reduction as abnormal except in the sense of a secondary shrinkage due to loss of fibers which normally would enter the pallidus from without. A question mark, then, in the globus pallidus in her cases seems fully as much in order as in Huntington's chorea.

As to the square devoted to paralysis agitans, some observers, e. g., Jelgersma, have claimed the existence of lesions in the nerve fiber systems of the globus pallidus, while J. Ramsay Hunt finds in juvenile paralysis agitans lesions in both the nerve cells and the fiber systems connected with this organ. Hunt's claims are discussed in the text, and Jelgersma's claims still need confirmation. It seems fair, then, to place a question mark opposite the cell and fiber systems of the globus pallidus in the paralysis agitans schema, especially as the nerve cell counts in the globus pallidus of this disease indicate, when compared with the controls (tables 1 and 2) at least no serious numerical loss of nerve cells; I have not investigated the quality of these nerve cells. The few personal observations at hand on the ansa lenticularis in type cases of this disease (three cases) show, in some instances at least, in agreement with Jelgersma and Hunt, a decided sclerosis in this system of fibers, but observations are too few as yet to justify any conclusions as to the constancy of a degeneration of this system in typical paralysis agitans.

PLATE 1


Anatomical Diagram
Caud. Nucl.
Putam.
Glob. Pall.
Corp. Luys.
Red N.
Monak. Bdl
Putam small cells.
Ansa Lentic
Thalam.
Red n.
H. Chorea: Site of Lesion.
?
?
No Tremors or Spasticity.
État Marbré: Site of Lesion.
neg ?
neg ?
Double Athetosis.
Wilson's Dis. Site of Lesion
ansa affected
Tremors, Spasticity
Paral. Agitans: Site of Lesion.
cells?
ansa affected ?
Tremors, Spasticity.

EXPLANATION OF PLATE 2

Plate 2.—Gross photographs, showing differences in size of the corpus striatum in a series of normal and abnormal basal nuclei. The cuts, with few exceptions, have been made either in an obliquely horizontal direction, usually through the anterior commissure and midthalamus in which the corpus striatum is exposed nearly in its full width, or in a transverse direction, through the anterior border of the foramen of Monro, in which the corpus striatum again is usually widest.

All gross measurements of the corpus striatum, as used elsewhere in the tables of this article, were made approximately at the levels here shown, and most of the microscopic examinations and nerve cell counts were made at these same levels as well as at other levels.

All of the photographs of this plate were taken natural size, and are reproduced from a photograph which was about two thirds the diameter of the originals.

Fig. 1.—Control specimen from a presumably normal (electrocution) case. The full sized basal nuclei, especially the corpus striatum, including the caudate nucleus, putamen and globus pallidus should be noted.

Figs. 2 and 3.—Transverse section of left hemisphere and horizontal section of right hemisphere, from a case of paralysis agitans. The basal nuclei here are considered to be of full size. Figure 3 shows a level slightly above the anterior commisure.

Fig. 4.—From a case of juvenile paralysis agitans, already reported by J. Ramsay Hunt. The anterior commissure is split in this section, but posteriorly the plane of section passes low through the base of the optic thalamus (external geniculate body) and the anterior corpora quadrigemina. This marked difference of level, as compared with the other specimens shown here, changes the shape and proportions of the putamen and renders the posterior part of this body, which is normally narrow and tapering at this level, not comparable with the rest of the series; the globus pallidus also looks relatively larger than at the usual level employed in this series. This section was fixed in solution of formaldehyde, followed by Muller's fluid for a few days.

Fig. 5.—Normal control (electrocution case). The level of section is slightly lower than in figure 1 and consequently the putamen is somewhat narrower.

Figs. 6 and 7.—Paralysis agitans. The left hemisphere is cut transversely, the right horizontally. The anterior commissure barely shows as a pale streak in the horizontal section. As in the other controls, the full, plump basal nuclei should be noted.

Figs. 8 to 12.—Four different cases of Huntington's chorea. Figures 8 and 10 are transverse sections and can fairly be compared with figure 6; figure 2 is cut too far forward to be strictly comparable with the choreas. In Huntington's chorea, the striking reduction in size of the corpus striatum in all its parts, both in the horizontal and in the transverse cuts should be noted. The optic thalamus is not plainly reduced in size. In figure 9, which was anatomically a marked case of Huntington's chorea, the level of section, although passing through the anterior commissure, was somewhat deeper than usual, thus causing the shrunken and reduced putamen to look even narrower than it would otherwise. In about the middle third are various small holes representing perivascular spaces. This case is further illustrated in the gross in plate 3, and microscopically in plate 6.

Designations: *a.*, Nucleus amygdalae; *a. c.*, anterior commissure; *c.*, caudate nucleus; *cl.*, claustrum; *g. p.*, globus pallidus; *g. e.*, external geniculate body; *i.*, island of Reil; *i. c.*, internal capsule; *e. c.*, external capsule; *p.*, putamen; *th.*, optic thalamus.

PLATE 2

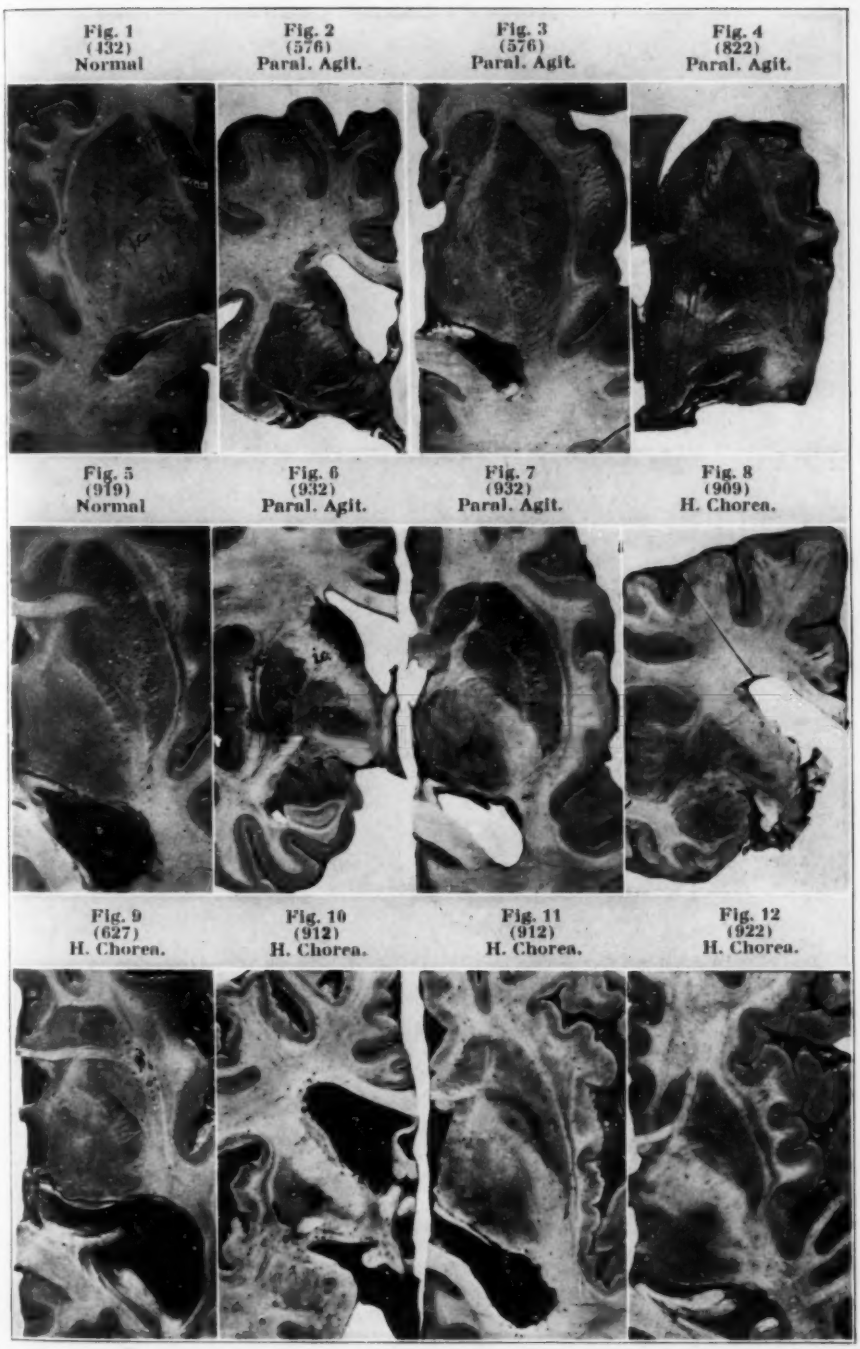


Fig. 1
(432)
Normal
Fig. 2
(576)
Paral. Agit.
Fig. 3
(576)
Paral. Agit.
Fig. 4
(822)
Paral. Agit.
Fig. 5
(919)
Normal
Fig. 6
(932)
Paral. Agit.
Fig. 7
(932)
Paral. Agit.
Fig. 8
(909)
H. Chorea.
Fig. 9
(627)
H. Chorea.
Fig. 10
(912)
H. Chorea.
Fig. 11
(912)
H. Chorea.
Fig. 12
(922)
H. Chorea.

Explanation of Plate 3

Plate 3.—Upper figure: A gross section cut semihorizontally of the two hemispheres of the brain in case 627, J. J., Huntington's chorea. This plate was reduced from a photograph which was natural size, and was viewed from below so that the sides are reversed. The cuts are made at different levels in the two hemispheres. The level of section is too high, even on the left, to expose the globus pallidus fully, while on the right, the globus pallidus is not seen at all.

This brain showed, more strikingly than any other in the series, the apparent reduction of white matter in Huntington's chorea; this reduction is especially well seen in the posterior half of this brain, in which the lateral ventricles are much enlarged. The gray matter, on the other hand, is approximately of normal thickness.

The substance of the left putamen looks somewhat withered and pitted. This should be compared with plate 2, figure 9, which shows the right basal nuclei of the same brain at a deeper level in which the pitting is marked. The microscopic changes in the putamen of the same case is shown in plate 6.

Lower figure: Horizontal section of the right corpus striatum, reduced from a photograph that had been magnified about 2½ diameters; Sims' stain; from case 912, J. M., Huntington's chorea showing the parts of the putamen most intensely affected in Huntington's chorea.

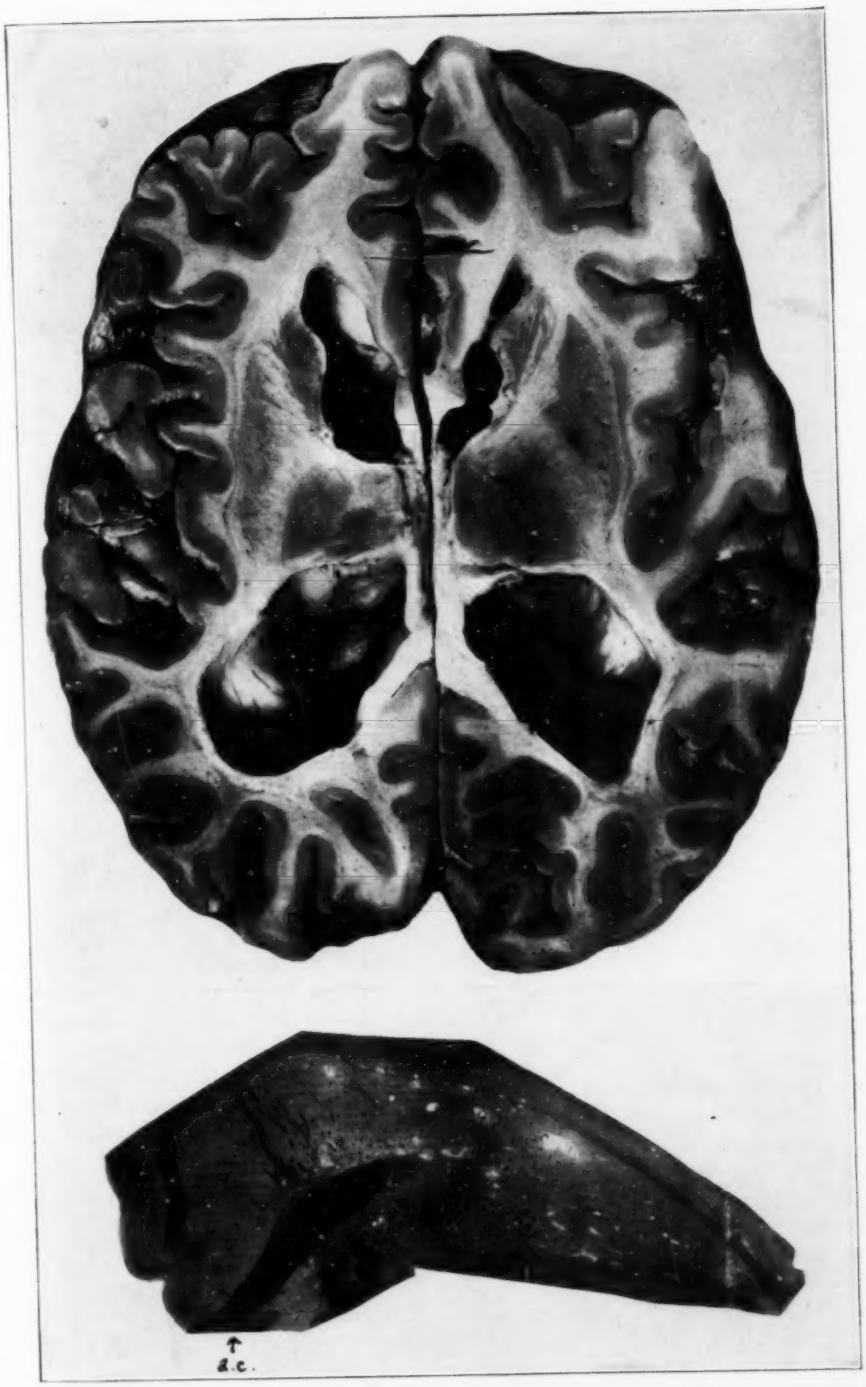
The section splits the large anterior commissure, *a. c.*, at a low level. The anterior and posterior limbs of the internal capsule are differentiated by the stain, also the putamen, the globus pallidus and the external capsule.

The caudate nucleus and about the anterior fourth of the putamen are fuller, sieve-like parts of the putamen which lies back of these. These paler parts comprise the region in which the loss of nerve tissue in Huntington's chorea is greatest.

Nerve cell counts, as shown in plate 4, and neuroglia stains unite in showing, in agreement with this illustration, that the caudate nucleus and the most anterior parts of the putamen, while not normal, are less affected as a rule in Huntington's chorea than are the middle and posterior parts of the putamen; the greatest loss of nerve cells is usually found at about the middle of the putamen.

The globus pallidus in this case (and in Huntington's chorea generally) is reduced in size; evidence of this is shown in plate 2, figures 10 and 11, which show this case in the gross in comparison with other cases. As far as can be determined, in Huntington's chorea, the nerve cell outfit of the globus pallidus, numerically at least, probably remains intact, but owing to the shrinkage in volume of this nucleus the cells lie nearer together than in a normal case; consequently the number of nerve cells seen in each microscopic field of the globus pallidus in Huntington's chorea is generally greater than in normal cases, the proportion being about 5 cells in Huntington's chorea to 3 in the controls, as shown in plate 4.

PLATE 3



Explanation of Plate 4

Plate 4.—The oval-shaped diagrams, in which the numerals are placed, represent the basal nuclei of the two sides of the brain as seen in horizontal section, with the anterior and posterior limbs of the internal capsule represented as heavy lines; thus, the caudate nucleus, the lenticular nucleus (including the putamen and the globus pallidus) and the optic thalamus are marked off. Plate one further explains these diagrams. The numerals in the different parts of the diagrams show the average number of nerve cells per microscopic field as found by actual count for the particular region. (The size of the miscroscopic field invariably used was approximately 0.24 sq. mm.)

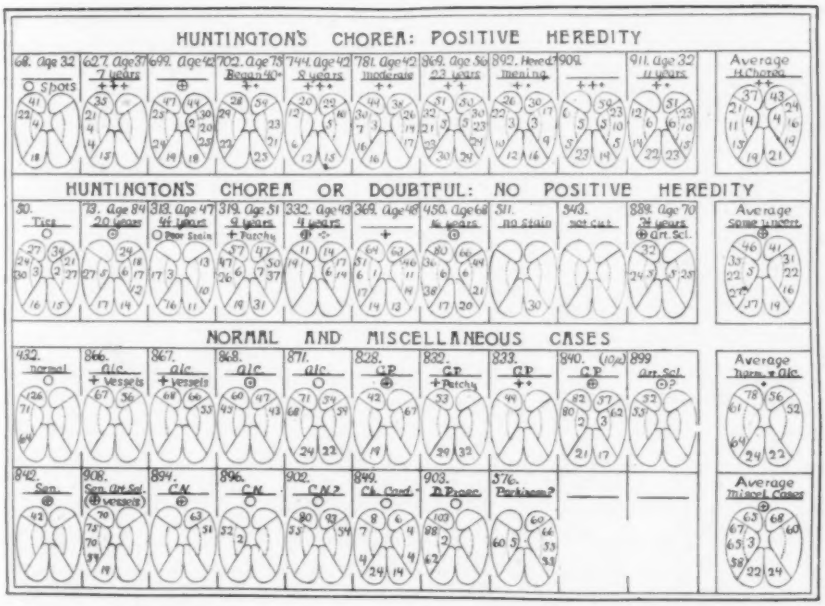
If one takes, for example, the first diagram in the chart, which is case 68, the patient being 32 years old at death, the number 41, situated in the left caudate nucleus, means that an average microscopic field in this nucleus contained 41 nerve cells. In other words, after several different observers had counted the nerve cells in many typical microscopic fields in this nucleus, the results were averaged and this number was obtained. The number 22, situated in the anterior third of the left putamen, represents likewise the average number of nerve cells per microscopic field, counted in that part of the putamen. The number 4 has a similar meaning for the left globus pallidus, and 18 for the left optic thalamus. As no counts were made on the right side in this case, that side is left blank.

Neuroglia changes were estimated, and the amount of reaction is indicated by signs placed above the diagrams, which apply to the corpus striatum as a whole. Three large plus signs (+++) denote an excessive neuroglia reaction. Two large plus signs (++) indicate less reaction than three, but still a marked reaction; one large plus (+) means a moderate reaction. A large and a small plus mean a reaction greater than one large plus, but less than two large plusses. A circle around a plus lessens the value of the plus and means a slight reaction. A dot within a circle means a slight neuroglia reaction; an empty circle means no reaction at all. The word "spots" after a sign means that the reaction indicated occurred in spots only.

On the right side of the chart as a whole, the individual groups of diagrams have been averaged in a column of larger diagrams, which give the average cell count and neuroglia reaction of each group of cases. One can thus see at a glance the striking differences which exist between the groups, namely, the positive Huntington group, with its small number of nerve cells and high neuroglia reaction, the doubtful Huntington group with a somewhat larger number of nerve cells and less neuroglia reaction, and the group of controls, with a much larger number of nerve cells in the putamen and a slight neuroglia reaction. Thus the number of nerve cells and the estimated neuroglia increase are epitomized for each group in a single diagram.

Minor errors in cell counts and in neuroglia estimates must, of course, exist in such a study, which deals with tissues in various states of preservation (good, bad and indifferent), but much care was used, and the margin of error does not vitiate the gross results which may be depended on as representing true conditions in our series of cases.

PLATE 4


HUNTINGTON'S CHOREA: POSITIVE HEREDITY
HUNTINGTON'S CHOREA OR DOUBTFUL: NO POSITIVE HEREDITY
NORMAL AND MISCELLANEOUS CASES

scope being included in the count. In different parts of this nucleus, there was considerable variation in the number and in the size of the nerve cells present, some fields containing a few cells and others a great many; I therefore felt that it was safer to count practically all the nerve cells in sections of the pallidus in order to get a fair average field, and I did so. Slight unavoidable variations in cutting the globus pallidus in a horizontal plane caused some differences in the average cell count of this organ; in Huntington's chorea, it tapers down mesially almost to a point, as may be seen in plate 2, figures 8 and 10, and it was difficult to strike it exactly in the plane desired and to get the required number of slices for embedding because, owing to the thinness here, one slice exhausted a large part of the available material.

Cell counts were not attempted in the red nucleus or in the hypothalamic nucleus; these structures were often not cut symmetrically, and I studied the normal conditions and variations in them too little to make such counts of much significance. In examining the two nuclei the usual impressionistic methods were used, and considerable dependence was placed on the presence or absence of neuroglia changes in estimating whether or not they should be considered normal.

Optic Thalamus.—Some general cell counts were tabulated for the optic thalamus, but they are too few to be important and should be disregarded in the table of diagrams.

Neuroglia.—In studying and recording the condition of the neuroglia in the corpus striatum, photographic illustrations, as shown in the accompanying plates, have been used in part, and impressionistic methods have been used in part. The results of the latter method are shown in the table of diagrams of the striatum (plate 4), in which plus and other signs have been placed just above each diagram to indicate slight or large estimated increases of neuroglia; the signs are explained in the legend that accompanies the diagrams, but, briefly, the greater the number of plus signs used the greater was the increase in neuroglia.

The blood vessels and connective tissues of the corpus striatum have not been illustrated except incidentally in photographs intended to show other things. As already stated, no changes in either of these elements were common to the group of choreas. Some cases showed a certain degree of arteriosclerosis, which was not unexpected, considering the ages of the patients at death, but in most cases the vascular apparatus grossly and microscopically was in a fair condition, and no gross focal softenings were found in any of the cases of Huntington's chorea.

METHODS OF EXAMINATION OF THE CORTEX

Examination of the cortex has proved a most perplexing task that is too far from completion to justify more than passing mention. The thickness of the gray matter in the cases of Huntington's chorea was measured not only grossly with the millimeter rule but also, in many undivided brains it was measured microscopically in stained sections with

a micrometer eye piece and a stage micrometer. Grossly, as a rule, no thinning of the gray matter was apparent in Huntington's chorea: this fact is shown fairly well in the photographs in plate 2, but in figures 10 and 11 of this plate, both of which are from a case of Huntington's chorea, the peculiarity of the formaldehyde fixation makes the gray matter as reproduced in the photograph look thinner than it actually was. Another example of the same peculiarity in fixation is seen in figure 12, in which part of the gray matter of the optic thalamus looks white. On the other hand, in the brains of the patients having Huntington's chorea which so far had been examined with the micrometer, the cortex on an average was slightly thinner than in the controls, but the difference was very little.

Comparison of the Cortex by Photographs.—The general architecture of the cortex, the condition of the various cortical layers, and the frequency of nerve cells was compared by means of photographs. These were made from sections cut from definite cortical areas in Huntington's chorea and from the same areas in the control material, as follows:

> From a definite cortical region in one of two brains which were to be compared, e. g., in a brain from a patient who had had Huntington's chorea, a thin slice for embedding was removed from a certain convolution, so that nerve cells and fibers would be struck parallel to their long axes. From the same region in the second or control brain a convolution similar in size and position was selected, and a similar slice was removed from it; these two slices were laid flat on a board, and each was divided in half by a straight razor cut which passed from top to bottom of each slice through the middle of the marrow. It was now possible to fit half of slice 1 (from the case of Huntington's chorea) so closely against half of slice 2 (from the control case) that the line separating the two was almost invisible and the two halves thus joined resembled a slice from a single convolution. The compound slice thus formed was embedded, cut, stained, studied with the microscope and photographed as a single specimen, with only a fine line dividing the cortex from the case of Huntington's chorea from that of the control.

The comparative photographs of sections of the brain as thus prepared were always made with the same magnification, with the bellows of the camera in a fixed position. Selection of the fields for illustration was left purposely to the photographer, who was unacquainted with the problem involved; the only directions given him were to photograph similar parts in each convolution, not the top of one and the side of the other, and to be sure that the fields seletced for photographs showed cells and fibers struck longitudinally, and not transversely or obliquely. Plates 9 and 10 show such comparative photographs. In each pair the left photograph is from the case of Huntington's chorea, and the right is from a control case.

In the cerebral cortex of the brains from the cases of Huntington's chorea, some comparative counts of nerve cells were also made. They

were made in narrow strips of cortex similar to those photographed; so far I have not been able to convince myself that there is any true loss of nerve cells in the cortex in the cases of Huntington's chorea (sometimes a higher number of cells was found in these cases than in the controls) and if any particular layer has suffered selectively I have not yet detected this but, as intimated, the whole question of the cortex needs a much more careful study than has so far been given it; I hope to carry this study further with better material. I have not yet found justification for the views of those who hold that in Huntington's chorea the cortex shows a developmental defect expressed in deficiencies in the layering, etc. The atrophy of nerve cells causes the layers to look different (i. e., more as if they were responsible for the fatal outcome).

The neuroglia tissue of the cortex so often failed to stain satisfactorily in both the control cases and in the cases of Huntington's chorea that it was not regarded as a trustworthy index of abnormal states in the nerve tissues here, however satisfactory it may have been as an index in the corpus striatum. In the cases of Huntington's chorea in which the neuroglia stains succeeded, neuroglia increase was the rule; this was often most marked in the deepest layers of the cortex, especially when cortex and marrow merged. Neuroglia stains in the corpus striatum were more successful than in the cortex.

WHITE MATTER

I have found no entirely satisfactory method of dealing with the white matter either grossly or microscopically. The weight of the cerebral hemispheres (as described below) is strikingly subnormal in Huntington's chorea, and if—as seems likely—there is only moderate loss of gray material, the white matter must of necessity account for the rest of the loss. Microscopically, accurate study of the great mass of white matter is almost hopeless. My material is unsuitable, owing to the age of most of it and the consequent deterioration in its staining qualities, for study of those systems of nerve fibers included within the gray matter of the cortex. In a few of the cases of Huntington's chorea, Weigert's myelin sheath stain has been used in studying the fiber systems in serial sections of the striatum and basal nuclei generally, and these sections have been compared with controls, especially with reference to the outgoing system of nerve fibers from the globus pallidus which are contained in the ansa lenticularis. No defect was discovered in this system. Moderate losses of white matter may easily escape detection by methods as coarse as this, especially when shrinkage in the volume of an organ like the pallidus (as described below) brings its systems of nerve fibers nearer together in a mass more compact than normally.

The whole volume of white matter, then, as compared with that of the gray, has remained an unsettled problem, and seems inaccessible.

In a few of the brains from the cases of Huntington's chorea (plate 2, figure 9), the white matter of the cerebral hemispheres grossly looked strikingly deficient in amount and the lateral ventricles were much enlarged; the gray matter, on the other hand, appeared to be normal in amount. In most cases, however, no such deficiency of white matter was apparent to the eye, but in practically every brain from a case of Huntington's chorea the scales showed a loss of brain substance in the cerebral hemispheres, the average loss being 174 Gm., a mass greater than that of the cerebellum, pons and medulla combined, an amount entirely too large to be accounted for by loss of gray matter which, for reasons given below, was probably slighter than the loss of white matter.

RESULTS OF STUDY BY THE DIFFERENT METHODS IN TRUE HUNTINGTON'S CHOREA

GROSS APPEARANCES

(*a*) In the cases of Huntington's chorea, the cerebral hemispheres, in all their parts both before and after section, were symmetrical. As a rule, the balances showed the right hemisphere to be a few grams heavier than the left. The pia mater did not present any constant gross changes; it was often somewhat thickened and hazy, especially over the top of the convexity, but this was not constant. The amount of fluid contained within it was variable, often of a considerable amount.

The blood vessels of the base of the brain and those of the convexity did not show any gross or microscopic characteristics that could be traced through the series. They were usually soft and strikingly free from atheroma, and were generally described as essentially negative. No inflammatory changes were seen either in the pia mater or in the blood vessels, with one exception (no. 744), in which Huntington's chorea was associated with the changes of general paralysis.

The cranial nerves were likely to be small, but they did not show any recognized gross abnormalities. The ependymal surfaces were free from granulations, except in the case of general paralysis to which I just referred.

On section, the brains from the seventeen cases of Huntington's chorea showed as the most striking feature (with an exception or two referred to later) a reduction in the size of the corpus striatum which involved all parts of this body while the consistency was well preserved. In other parts of the brain, the cortical and medullary tissues were firm and appeared well preserved; no foci of softening were found in any of the cases of Huntington's chorea.

(*b*) The cerebral hemispheres from the cases of Huntington's chorea were as a rule subnormal in weight, while the cerebellum was of full

size. The loss of weight in the cerebrum was greater than the whole mass of the cerebellum, pons and medulla oblongata combined. This loss probably involved chiefly the white matter, while the gray matter was less reduced.

TABLE 1.—*Huntington's Chorea; Positive Cases*

Case Number Institute Records	Total Weight of Brain, Gm.	Weight of Parts of Brain: Left Hemisphere	Right Hemisphere	Cerebellum	Proportion of Cerebellum to Cerebrum	Gross Measurements of Corpus Striatum: Left Transverse	Right Transverse	Left Longitudinal	Right Longitudinal	Putamen: Transverse Measurements: Left	Right	Nerve Cells per Field in Globus Pallidus: Left	Right
34	765	330	330	105	1 to 6.3	11	10.5	33	34	4	4	0	8+
67	1,050	455	445	150	1 to 6	11	0	34	0	5	0	0	5.5
68	907	380	380	147	1 to 5.2	12	12	0	35	5	5	5+	0
627	1,267	547	518	202	1 to 5.3	0	12.5	0	33	0	4.5	4.5	0
699	1,005	440	450	115	1 to 7.7	15	14	32	33	7.8	7	0	3.6
702	899	380	392	127	1 to 6.1 (?)	12	11	0	34	?	5	0	3—
744	1,027	435	450	142	1 to 6.2	12	10	31	31	4	4	5.6	5.3
781	985	415	430	140	1 to 6	13	13	35	32	6	6	5	5
869	840	350	360	130	1 to 5.5	14	14	35	35	6	6	5	4.5
892	922	385	400	137	1 to 5.7	0	0	0	0	0	0	3.5	3.2
909	767	320	330	117	1 to 5.5	0	11	0	0	0	0	4.4	4.6
911	913	395	390	128	1 to 6.1	0	11	0	0	0	4	5.8	5.5
912	1,120	470	460	190	1 to 4.9	0	13.5	0	35	0	5.5	0	0
922	1,245	525	525	195	1 to 5.4	0	12	0	32	0	6.5	6.9	6.6
Aver.	980—	416	419	145	1 to 5.8	12.5	12	33.3	33.4	5.4	5.2	5.1	5.2

TABLE 2.—*Miscellaneous Control Cases*

Case Number Institute Records	Total Weight of Brain, Gm.	Weight of Parts of Brain: Left Hemisphere	Right Hemisphere	Cerebellum	Proportion of Cerebellum to Cerebrum	Gross Measurements of Corpus Striatum: Left Transverse	Right Transverse	Left Longitudinal	Right Longitudinal	Putamen: Transverse Measurements: Left	Right	Nerve Cells per Field in Globus Pallidus: Left	Right
432	1,097	450	510	137	1 to 7.0	0	20	0	37	0	10	3.7	3.6
806	1,039	465	453	121	1 to 7.6	20	20	0	0	9	9	3.3	3.2
867	1,107	480	495	132	1 to 7.4	0	19 (?)	0	0	0	0 (?)	3.5	3.8
868	980	435	430	115	1 to 7.5	19	18	37	37	9	8	3.1	3.2
871	959	417	420	122	1 to 6.9	0	0	0	0	0	0	3.5	3.5
875	1,178	523	503	152	1 to 6.7	18	20	42	36	9	10	0	0
891	1,136	484	497	155	1 to 6.3	18	18	37	35	8.5	10	0	0
897	1,251	543	553	155	1 to 7.1	0	0	0	0	0	0	0	2.5
902	1,069	465	468	133	1 to 6.9	0	0	0	0	0	0	2.8	3.1
903	1,166	516	532	118	1 to 8.9	16	0	38	0	6	0	2.5	0
905	1,198	513	522	162	1 to 6.4	19	19	37	37	11	11	0	0
906	1,126	500	500	126	1 to 7.9	0	0	0	0	0	0	0	0
917	1,338	584	583	171	1 to 6.8	0	18	0	38	0	7	0	0
919	1,502	668	668	171	1 to 7.8	20	20	43	43	10	10	0	0
Aver.	1,153	503	510	141	1 to 7.2	18.6	19.1	39	37.6	8.9	9.3	3.2	3.3

The individual brains in the group of cases of Huntington's chorea showed features essentially common to the group as a whole. Comparative weights, as given in tables 1 and 4, clearly show that the average brain in the cases of Huntington's chorea weighed 980 Gm.; this is

decidedly smaller than the average brain in the control cases, which weighed 1,153 Gm. The weights show that this smallness is not due to generalized decrease in all parts, but that it is due to decrease in the forebrain or cerebrum only. The weights imply not only the presence of atrophy in the forebrain but also roughly the amount of atrophy present. The cerebellum, which is practically of normal size in Huntington's chorea, appears large in comparison with the small cerebrum.

TABLE 3.—*Huntington's Chorea: Eight Doubtful Cases with Averages*

		Weight of Parts of Brain				Gross Measurements of Corpus Striatum				Putamen: Transverse Measurements		Nerve Cells per Field in Globus Pallidus	
Case Number Institute Records	Total Weight of Brain, Gm.	Left Hemisphere	Right Hemisphere	Cerebellum	Proportion of Cerebellum to Cerebrum	Left Transverse	Right Transverse	Left Longitudinal	Right Longitudinal	Left	Right	Left	Right
50	1,087	485	470	132	1 to 7.2	13	13	35	35	7	7	2.5	3.3
73	874	375	380	119	1 to 6.3	14	14	35	35	7	7	5.5	5
313	1,027	445	435	147	1 to 6	14	13	33	33	7	6	0	0
319	1,016	434	440	142	1 to 6.2	15	16	36	35	7	6	5	4
332	1,050	445	460	145	1 to 6.2	0	0	0	0	0	0	5.5	5.5
369	845	355	363	127	1 to 5.6	10	11.5	35	37	6	4.5	6.4	6.4
450	1,339	582	600	148	1 to 8	20	19	40	39	8	7.5	0	3.4
889	927	400	405	122	1 to 6.6	0	16	36 (?)	38	0	7	4.5	5
Aver.	1,020	440	444	135	1 to 6.5	14.3	14.6	36	36	7	6.4	4.9	4.7

TABLE 4.—*Averages Including Positive and Doubtful Huntington's Chorea and Miscellaneous Cases*

		Weight of Parts of Brain				Gross Measurements of Corpus Striatum				Putamen: Transverse Measurements		Nerve Cells per Field in Globus Pallidus	
	Total Weight of Brain, Gm.	Left Hemisphere	Right Hemisphere	Cerebellum	Proportion of Cerebellum to Cerebrum	Left Transverse	Right Transverse	Left Longitudinal	Right Longitudinal	Left	Right	Left	Right
Huntington's chorea positive	980	416	419	145	1 to 5.8	12.5	12	33.3	33.4	5.4	5.2	5.2	5.2
Huntington's chorea doubtful	1,020	440	444	135	1 to 6.5	14.3	14.6	36	36	7	6.4	4.9	4.7
Miscellaneous (control) cases	1,153	503	510	141	1 to 7.2	18.6	19.1	39	37.6	8.9	9.3	3.2	3.3

The average weight of the cerebellum in the series of cases of Huntington's chorea was 145 Gm., while the weight of the cerebrum averaged 835 Gm.; this makes a proportion of about 1 to 5.8, while the proportion found in the series of control cases was about 1 to 7.2.

Sometimes it was plain on inspection that the cerebral hemispheres were small as compared with the cerebellum, and this first suggested

weighing the cerebrum and cerebellum separately. The medulla oblongata was included in the weight of the cerebellum and the midbrain was included in the weight of the cerebrum, but as this was true in all brains examined the results are comparable.

According to the figures in table 2, the cerebrum normally [10] should weigh a little more than seven times as much as the cerebellum; in the chorea cases then, with a cerebellum averaging 145 Gm., the cerebrum, if normal, should average about 1,040 Gm. instead of 835 Gm., which was the average actually found. Thus it is seen that the loss of weight in the forebrain in the cases of Huntington's chorea (about 200 Gm.) is greater than the whole mass of the cerebellum and medulla oblongata combined. In Huntington's chorea, as stated, the average proportion of cerebellum to cerebrum was one to five and eight-tenths (1:5.8) instead of one to seven and two-tenths (1:7.2), which was the proportion found in the control cases. From these facts, one might infer that the essential disease process in Huntington's chorea is more likely to be found in the atrophied cerebrum than in the full sized cerebellum.

In a rough way, the amount of atrophy in the forebrains in the cases of Huntington's chorea can be calculated for each case (if the exceptional case 699 is omitted) by multiplying the weight of each cerebellum, as given in table 1, by seven and two-tenths (7.2), which gives approximately what the cerebral hemispheres, if normal, should weigh. The fifth case (699) in the tabulated series of cases of Huntington's chorea is plainly an exception to the foregoing rule of proportions.

There is no doubt that this patient, W., a farm laborer, aged 42, from the Hudson River State Hospital, who died in 1911, had genuine Huntington's chorea. He came of a family not only that was choreic but that was of inferior grade as well. The grandfather, father, three paternal uncles, two brothers and one sister had chorea. The patient had been of decidedly inferior grade before the chorea developed and had been able to acquire only a little knowledge in school. Eight years before death he was nervous, but was a good worker. In the last four years of life he had been unable to do any consecutive work and finally even needed assistance in dressing. He stated that he had been half crazy for two or three years, but others had noticed mental symptoms only about five months before death. He died suddenly and unexpectedly in his chair.

The forebrain weighed 7.7 times as much as the cerebellum, but this was explained by the fact that the cerebellum, including the pons and medulla oblongata, was obviously abnormally small even on gross inspection; on microscopic examination, it was plain that the individual folia were atrophied and were different from those in the other cerebellums of the series of cases of Huntington's chorea. The Purkinje cells in this cerebellum were present

10. It is desirable to repeat that the control material is not in any sense normal; it is, however, nonchoreic. Probably a comparison of the brains from cases of Huntington's chorea with really normal controls would only exaggerate the differences shown to exist in the material at hand.

in about normal numbers; the thickness of the so-called molecular layer was even greater than in the controls, but the cerebellar marrow was decidedly narrow and much reduced in amount, and the atrophy had evidently come mainly from this source. The reduced marrow also contained an excess of neuroglia nuclei, and an increase of coarse neuroglia fibers.

The corpus striatum of this case was also exceptional in the series of cases of Huntington's chorea, as the measurements in table 1 show; although it was small, it was more nearly normal in size than in the other cases, and the thickness of the putamen approached that of the controls. The number of nerve cells in the putamen was reduced, as elsewhere in the series (this is discussed in the following section), but the reaction here on the part of the neuroglia was by far the slightest seen in any of the cases of Huntington's chorea charted, except the first and last cases of the chart, in which the neuroglia stain was, for certain reasons, as will be discussed later, a complete failure in all parts of the brain. The globus pallidus in this case is also irregular in view of the fact that the nerve cell count resembles that of the controls.

The marked cerebellar atrophy — the only instance of this in the series of cases of Huntington's chorea — easily explains the exceptional proportion between cerebrum and cerebellum in this case, so that anatomically the case as a whole is not as inconsistent with the rest as it at first appears to be. Atrophy is present in the corpus striatum as a whole, which is a feature regularly present in Huntington's chorea, but the atrophy is of slighter grade than in the other cases of this disorder. There is also a loss of many nerve cells in the putamen, which also, as will be seen below, is a constant feature. Nevertheless, the possibility of cerebellar influence in the production of choreic complexes, as claimed by Bonhoeffer,[11] Monakow[12] and others, is raised by such a case and must not be lost sight of. Death was sudden and unexpected, mental abnormalities had been noticed for only a few months and the possibility that this case had not progressed as far or as rapidly as the others must also be remembered.

In another case, 892, the tenth in the series of cases of Huntington's chorea, as seen in table 1, an exceptionally low nerve cell count was also found in the globus pallidus—a count like that seen in the controls. In this case the usual measurements of the corpus striatum were not made, but it was described as "small." The brain looked boggy, and there was a marked purulent meningitis. This patient, Mrs. D., was a sister of the patient in the thirteenth case in the series (912). The brain follows the rules in the cases of Huntington's chorea with the exception of the low cell count in the globus pallidus, for which I have no explanation.

These two cases (the fifth and tenth in the series of cases of Huntington's chorea), which present some exceptional features, are

11. Bonhoeffer, K.: Ein Beitrag zur Localisation der choreatischen Bewegungen, Monatschr. f. Psychiat. u. Neurol. **1**:6, 1897.

12. Von Monakow, C.: Experimentelle u. path.-anat. Untersuchungen über die Haubenregion, den Sehhügel u. die Regio subthalamica, nebst Beiträgen zur Kenntniss früh erworbener Gross- und Kleinhirndefekte, Arch. f. Psychiat. **27**:1 and 386, 1895.

not sufficiently atypical to call for further comment, and are regular in regard to the loss of nerve cells in the putamen. Why the cell count in the globus pallidus was low in both cases as it was in the controls was not determined.

There are reasons for believing that the loss of weight in the forebrain in Huntington's chorea takes place mainly but not wholly at the expense of the white matter. To the measuring scale, the gray matter seems approximately as thick as in the controls. This does not mean that the gray matter is present in normal amount, for it is obvious that if two brains were alike in everything but size, less gray matter of normal thickness would be required to cover the surface of a small cerebral hemisphere, such as that in Huntington's chorea, than of a large one, on the principle that less material of the same thickness would be needed to cover a cherry than to cover an orange. In a few individual cases of Huntington's chorea, gross inspection showed that the white matter was unquestionably much reduced in volume as compared with the gray; this is shown in plate 3, figure 1, and it seemed highly probable, as a result of calculations based in part on planimeter measurements, that in the series of cases of Huntington's chorea the loss of weight was mainly a loss of white matter rather than of gray. Cruickshank,[13] in trying to ascertain the relative proportions of white and gray matter in human brains by actual dissection, always found a preponderance of gray matter in the normal cerebral hemispheres, about 55 per cent of the whole mass being gray. He also found that in atrophic conditions the loss of white matter was relatively greater than the loss of gray matter, and the greater the degree of atrophy the greater was the disproportion between the white and gray.

(*c*) Gross measurements of the corpus striatum in Huntington's chorea showed this organ to be, on an average, less than half as large as in the control cases. All parts of the striatum appeared to take part in this reduction in size.

On inspection, no significant reduction was noted in the size of the optic thalamus.

In tables 1 and 2, not only are the comparative weights of different brains shown, but also the results are given of gross measurements of the corpus striatum in Huntington's chorea in comparison with controls. It will be seen, by reference to these tables, that in Huntington's chorea the corpus striatum is always small and the width is more reduced than the length; the narrowness of the putamen is especially noticeable. The columns of averages in these tables bring out clearly the striking differences in the size of this organ in the group of choreas when com-

13. Cruickshank, John: The Relative Amounts of Gray and White Matter in Some Normal and Pathological Brains, Rev. Neurol. & Psychiat. **15**:1, 1917.

pared with the group of controls; the average putamen in the control cases is nearly twice as wide as in the series of cases of Huntington's chorea. The somewhat exceptional case (699), the fifth in the cases of Huntington's chorea, has already been discussed.

Plate 2 supplements this table of measurements by showing in comparative photographs the smallness of the striatum in some of the cases of Huntington's chorea. These photographs were all taken natural size and are all equally reduced in the reproduction. The horizontal

TABLE 5.—*Miscellaneous Cases by Diseases*

Diagnosis	Case Number*	Source	Age of Patient	Atrophy of Brain	Nerve Cells in Globus Pallidus		Comment
					Left	Right	
Normal cases.....	432 ♂	Prison	25+?	None	3.7	3.6	
(electrocution)	897 ♂	Prison	19+	None	...	2.5	
Alcoholic cases.....	866 ♂	King's Park	75	Slight	3.3	3.2	Arteriosclerosis of small vessels
(Korsakoff)	867 ♂	King's Park	62?	Slight	3.5	3.8	Arteriosclerosis of small vessels
	868 ♂	King's Park	59	Plain atrophy	3.1	3.2	Arteriosclerosis; few senile plaques
	871 ♀	King's Park	64	General atrophy	3.5	3.5	Arteriosclerosis of small vessels
General paralysis..	828 ♂	Institute	58	Slight	2.7	2.5	Some endarteritis
	832 ♂	Institute	46	Moderate	2.7	2.7	Much neuroglia in deep cortex
	833 ♂	Utica S. H.	42	Marked frontal	3.3	2.8	Marked case: much neuroglial reaction
	840 ♀	Cent. Islip	49	General and local	4.4	...	Asymmetrical; left hemisphere small and atrophic
Central neuritis....	804 ♀	Willard	57	Slight	3.0	3.2	Typical cell changes
	896 ♀	Manhattan	29	None	4.1	...	Typical cell changes
	902 ♂(?)	Long Isl.	75	Frontal and central	2.8	3.1	Atypical: perivascular neuroglia
Senile dementia with plaques	842 ♀	Cent. Islip	71	Marked	3.8	3.5	Aphasia: many senile plaques
	908 ♀	Cent. Islip	50 ?	Marked	3.2	3.0	Many senile plaques; small vessels thick
Dementia praecox?	903 ♀	Dr. Ricksher	26	Slight or absent	2.5	...	Fairly normal looking brain
Unknown case.....	918 ?	?	?	?	...	2.5	Nothing known of hist.
Gas poisoning.....	138 ?	Dr. Hunt	?	Probably none	3.2	...	No history available
	428 ?	Dr. Ewing	?	Probably none	2.1	2.2	No history available
Paralysis agitans..	576 ♂	Middletown	67	Slight	3.7	4.0	Somewhat atypical
	822 ♂	Dr. Hunt	40 ?	None apparent	3.0	...	Juvenile case (reported by Dr. Hunt)
	926 ♂	Dr. Hunt	53	Not determined	3.3	3.1	Ordinary case
	927 ♂	Dr. Hunt	61	Not determined	3.2	...	Ordinary case
Average.....					3.2	3.1	

* In this column, ♂ indicates male; ♀, female.

views (figs. 9, 11 and 12) show well the reduction in size of the putamen in Huntington's chorea, but the transverse views (figs. 8 and 10) show especially well the reduction in size of the striatum as a whole, including the caudate nucleus, the putamen and the globus pallidus.

Only a small part of the loss of weight in the forebrain in Huntington's chorea can be accounted for by the smallness of the corpus striatum, for in control brains of average size (table 6), the combined weight of the two corpora striata was found to be only about 25 Gm.;

this organ was reduced to less than half its normal size in the cases of Huntington's chorea, but the total loss from this source would hardly exceed 15 Gm., while the average loss of substance in the cerebrum is more than ten times that amount.

In order to ascertain in figures the approximate loss in volume of the striatum in the group of cases of Huntington's chorea, the volume of the lenticular nucleus was found by calculations which were based on the average length and breadth as given in table 1, and the thickness was measured separately; the volume of this organ in the controls was calculated in the same way. The same set of measurements was also used in a rough reconstruction, in modeling clay, of the lenticular nucleus in each group of cases. The two models were then separately weighed. The weights thus obtained represented the proportionate mass of the lenticular nucleus in the controls to that in the choreas, and the

TABLE 6.—*Comparison of Weight of Normal Corpus Striatum and Optic Thalamus to Whole Brain*

	Weight of Brain, Gm.	Weight of Corpus Striatum in Gm.		Per Cent of Corpus Striatum to Brain	Weight of Thalamus		Per Cent of of Optic Thalamus to Brain	Corpus Striatum and Thalamus, Combined, to Brain
		Left	Right		Left	Right		
I	1,100	10.5	10.5	2 1:52.4	....	....	....	.....
II	1,072	10.5	....	2 1:51	8	7.5	1½ 1:69	3½
III	1,388	15.3	....	2 2 1:45.3	10.3	....	1½ 1:67	3 7/10

weights agreed closely with the calculations of volume; they showed that the striatum in the choreas was probably less than half as large as the striatum in the controls, the actual figures being 1 to 2.3. There is no pretense that these proportions are more than approximately correct;[14] they are based on the lenticular nuclei only; the caudate nuclei are so drawn out and so irregular in form that attempts to calculate their volume would be of little value in my hands, so a part, the lenticular nucleus, has been used to represent the whole.

In three miscellaneous control brains, whose average individual weight was 1,187 Gm., the actual weight of the corpus striatum was determined by dissecting it out by means of cutting around its borders in thin serial slices, collecting the pieces and weighing them (table 6).

14. I have constantly found throughout this work that measurements, weights and counts could be only approximations, that accuracy in the strict sense was not obtainable, and that the margin of error, or of unavoidable variation, was everywhere considerable, but I feel that the number of cases examined and tabulated has largely neutralized unavoidable errors in individual cases and that the facts stand out with unquestionable clearness notwithstanding the impossibility of obtaining absolutely accurate measurements and weights or absolutely accurate cell counts.

This method gave approximately 12.5 Gm. as the weight of the striatum in each hemisphere of a medium sized, nonchoreic brain, or 25 Gm. for both striata, a weight which is about one forty-seventh of the total weight of such a brain, or approximately 2 per cent (table 6).

The optic thalamus was not measured or weighed in the series of cases generally, but on gross inspection it did not seem unusual in any way in Huntington's chorea. In two of the control cases (table 6) in which it was dissected out and weighed separately, the results were approximately 16 Gm. for the combined weight of the two optic thalami in a brain which weighed 1,072 Gm., and 10.3 Gm. in one hemisphere of a brain which weighed 1,388 Gm. In other words, the thalamus in each of these brains was about one sixty-eighth of the weight of the whole brain, or roughly 1.5 per cent of the weight of the brain, while the striatum, as seen above, was larger than the thalamus.

Summary.—Grossly, then, the brains in the positive cases of Huntington's chorea were small and were of diminished weight, the reduction being chiefly if not entirely in the forebrain, which showed evidence of marked general atrophy affecting the convolutions, the deep marrow and especially the corpus striatum, which was less than half the normal size. There were no significant changes in the pia mater or in the blood vessels. The gray matter was of good thickness though probably reduced in actual amount; the white matter was usually considered to be more reduced in amount than the gray. In the optic thalamus nothing unusual was found, but here the examination was not sufficiently thorough. The cerebellum was regarded as essentially normal in all cases except one and its average weight equalled that of the controls, but further study is needed here also. No conclusions were reached regarding the other basal nuclei.

(*d*) The nerve cells in all parts of the putamen of Huntington's chorea, especially in the middle and posterior parts, were regularly reduced in number as compared with the controls—sometimes a very few nerve cells remained.

The nerve cells in the caudate nucleus of Huntington's chorea were also regularly reduced in number, but not to the great extent seen in the putamen.

Not only was the whole corpus striatum in true Huntington's chorea regularly small, but also the nerve cells in the caudate nucleus and especially in the putamen were much reduced in number in all of the cases; they were so greatly reduced in some of the cases that in certain microscopic fields, in which normally sixty or more nerve cells would be present, only two or three might be found [plate 4 gives diagrams showing the average nerve cell counts referred to under (*c*)]. The disorganization of the striatum from loss of nerve cells was usually

greatest in about the second and third fourths of the putamen, with better preservation in the anterior end of this nucleus, and sometimes slightly better preservation in the posterior end.

The caudate nucleus, although many of its nerve cells had disappeared, was regularly less disorganized than the putamen. These two nuclei in structure closely resemble one another and are almost certainly only parts of a single nucleus, which have been incompletely separated by the anterior limb of the internal capsule. Frequent bridges of gray matter, passing across this portion of the capsule, still connect them; some of these bridges are seen in plate 2, figure 4.

The loss of nerve cells in the caudate nucleus and putamen of Huntington's chorea—great as it appears to be in the plate of diagrams—is even greater than the counts with the microscope would indicate. One is counting cells in an organ that has shrunken to about half its normal volume; consequently, the nerve cells remaining in this reduced area must lie nearer together and therefore must be more abundant in each microscopic field than if the organ had remained of full size. The effects of reduction in the volume of an organ on the frequency of nerve cells contained within it will be referred to again and again, especially in discussing the nerve cells in the globus pallidus and in the cortex. In the group of questionable cases of Huntington's chorea, a loss of nerve cells in the putamen was also a well marked feature, as shown by the table of diagrams in plate 4.

In plate 3, figure 2 is a photograph of a horizontal section from the striatum in Huntington's chorea; the first or anterior fourth of the putamen here looks fairly compact and dense, but the paler coloring and the more open structure of the second and third fourths mark the parts of this nucleus which are usually most seriously affected in this disorder, though the posterior end may be just as severely involved. The table of diagrams (plate 4) shows the same thing by numbers, as the smallest number of nerve cells is usually found in the central part of the putamen. The same part, or rather the middle third, of the putamen was also the part most affected in Wilson's [4] cases of progressive lenticular degeneration to be referred to later.

(*c*) The nerve cells in the globus pallidus of Huntington's chorea (with two exceptions) were regularly more numerous, field for field, than in the control cases.

The globus pallidus normally presents an entirely different type of structure from the caudate nucleus and putamen, and a different type of nerve cell; none of the small nervous elements of the putamen and caudative nucleus appear here.

It was at first a surprise to find an increased number of nerve cells per microscopic field in the shrunken globus pallidus of Huntington's chorea, as shown in plate 4, and in tables 1, 2 and 3 in which the propor-

tion is approximately five cells in the pallidus of the choreas to three in the controls. As has already been stated, this part of the striatum, as well as the other parts, is markedly reduced in volume in Huntington's chorea. Plate 2, figures 8 and 10, shows the proportions of this reduction. It seems certain that this shrinkage in size of the globus pallidus is not due principally to loss of nerve cells, but rather to loss of intercellular material; this intercellular loss brings the cells themselves nearer together as the organ shrinks in size, thus increasing the number of nerve cells contained in each microscopic field. It is certain, moreover, that intercellular material has disappeared from the globus pallidus in Huntington's chorea for the small nerve cells of the putamen and caudate nucleus, especially the former, are known to send out great numbers of nerve fibers into the globus pallidus, which end there. The wholesale destruction of the small nerve cells in both the putamen and caudate nucleus, as in Huntington's chorea, results in wholesale destruction of their fibers including those which enter the globus pallidus, for one may accept as axiomatic the statement that when one of these nerve cells is destroyed, its fiber is also destroyed.

Whether there are any defects in the globus pallidus of Huntington's chorea other than reduction in size due to loss of nerve fibers entering from without has not been satisfactorily determined; whether the total amount of shrinkage in this nucleus can be accounted for by this loss of nerve fibers alone is also a question. No method was found by which to determine whether any loss of nerve cells had occurred in the pallidus; such a loss of nerve cells would be a possibility in spite of the apparent increase in number through concentration into a smaller space, but it does not seem probable that any loss exists, as appears below.

The neuroglia in the globus pallidus was usually somewhat increased in amount and looked overactive; this, however, might be expected in view of the loss of intercellular material as shown in the foregoing. The size and internal structure of the nerve cells themselves has received little attention for reasons already given, but the ansa lenticularis, a considerable part of whose fibers are derived from the large nerve cells of the globus pallidus, stained deeply and well in Weigert preparations of specimens from cases of Huntington's chorea and was regarded as probably normal when compared with the controls.

Summary.—The scope of the examination of the globus pallidus did not disclose any real evidence of primary disease, and the reduction in size appeared to be due largely, if not wholly, to secondary causes, but it is not possible to say that the entire nerve cell outfit of the pallidus is intact.

(*f*) The fibrous neuroglia in the corpus striatum of Huntington's chorea as a rule was much increased in amount; it was coarse and fibrous in character, and was most abundant in those parts in which loss of

nerve cells was greatest. The nuclei of the neuroglia cells associated with the hypertrophied neuroglia fibers were much larger than those of normal neuroglia. Neuroglia nuclei of normal size were much increased in number.

In the corpus striatum of Huntington's chorea, increase in the amount of neuroglia or some change in its normal characteristics is believed to be a constant feature and one that might be expected in view of the loss of nerve tissue. The technical difficulties, however, of staining and demonstrating the complete neuroglia outfit of any organ are well known, and all who have used the various staining methods know how uncertain and capricious the results are. Consequently, in tabulating the results of the examination of the neuroglia in the striatum, which has been attempted in plate 4 by the use of signs, some explanations are called for and reasons should be given for leaving out certain numbers of the group of cases of Huntington's chorea (namely, 34, 67 and 922) in the general summing up of results.

In the three oldest brains of this group, 34, 67 and 68, all of which had been in formaldehyde solution from twelve to thirteen years, the neuroglia fibers in the corpus striatum and elsewhere practically failed to stain at all, or succeeded only slightly in occasional spots, but in all these cases an increase of small round neuroglia nuclei to more than twice the normal number was plainly present. The same increase in neuroglia nuclei was found by Alzheimer in his cases of Huntington's chorea, but he does not mention increase in the fibrous neuroglia, which in most of my cases was a most striking feature. In case 911, the last one tabulated in the table of diagrams, plate 4, the stain for neuroglia fibers was a total failure; all of the tissues looked powdery or granular, and no information whatever concerning the fibers could be gained from this stain, though the neuroglia nuclei were in excess. It is therefore considered unfair in the summing up to use either this case or the three just mentioned as showing absence of fibrous neuroglia reaction in Huntington's chorea; they showed absence of stain, not absence of fibers, and should properly be labelled failures for technical and other reasons; they should be omitted in the final summing up, as has been done. The large excess of neuroglia nuclei in these four cases may mean little as to real neuroglia reaction, because the general shrinkage in volume of the striatum in Huntington's chorea would mechanically bring the neuroglia nuclei nearer together, and thus an abnormally large number of such nuclei would appear in each microscopic field. For want of space, all of the cases of Huntington's chorea could not be included in the table of diagrams. Accordingly, the two oldest brains, 34 and 67, in which the neuroglia stained poorly, were left out. Brain 68 probably should have been omitted also for similar reasons and

on account of the length of time it had been in formaldehyde solution, which is the same as case 67, but was left in the table as an example of the older material. These old brains cannot, of course, be fairly compared as to neuroglia fibers with fresher brains for the reasons already given (poor stainability, etc.), but the number of nerve cells in the older and newer material, if well stained, are strictly comparable, as were the neuroglia cells.

In all of the seventeen positive cases of Huntington's chorea, with the four exceptions mentioned, in which the evidence was not complete through failure to stain, and the exceptional case (699), with a small cerebellum, there was a pronounced fibrous neuroglia reaction, as well as an apparent increase in the number of neuroglia cells in the corpus striatum; this was especially marked in the putamen but was also present in the caudate nucleus and to a less degree in the globus pallidus.

These changes in the putamen are shown in plate 6, the lower two figures, plate 7, upper figure and plate 9, both figures. These figures show a coarse hypertrophied condition of many neuroglia fibers with large vesicular neuroglia nuclei associated with such fibers. Sometimes, as in plate 7, the fibers are seen to radiate from small groups of such neuroglia nuclei, whose size, grouping and general appearance suggest a state of activity, while the majority of the neuroglia nuclei, which are of the smaller, dark-staining variety, are suggestive of a quiescent state. The strikingly small number of nerve cells is apparent in these photographs, all of which are from the putamen. Not one of these photographs should contain less than fifty nerve cells if taken from normal brains. For a control case compare plate 5 taken from a case of chronic alcoholism, the lower figure of which shows in sufficient magnification approximately the normal frequency of nerve cells in this region.

The increase of fibrous neuroglia was greater in the putamen than in the caudate nucleus or in any other part of the brain, and was greatest in those parts of the putamen in which the loss of nerve cells was most complete. The reaction thus followed closely in distribution the areas of greatest loss, of nerve cells, being more extreme when nerve cells were fewest and fading out in intensity as nerve cells became more abundant. In the striatum, it was consequently greatest in the middle and posterior parts of the putamen and least in the caudate nucleus.

It was striking to see how translucent and how open and loose in structure some of the areas of greatest degeneration were; little was left except the framework of the tissue, composed chiefly of capillaries and connective tissue with coarse neuroglia fibers extending among them, while the filling-in material, so to speak, or the nerve parenchyma, which gives body and compactness and density to normal nerve tissue of this region and prevents the light from readily passing through, was practically absent.

EXPLANATION OF PLATE 5

Plate 5.—Sections from the right putamen in case 867, J. E., alcoholic psychosis and arteriosclerosis; Sims' stain. The photographs show about the normal frequency of nerve cells as seen in the putamen of the ordinary control cases.

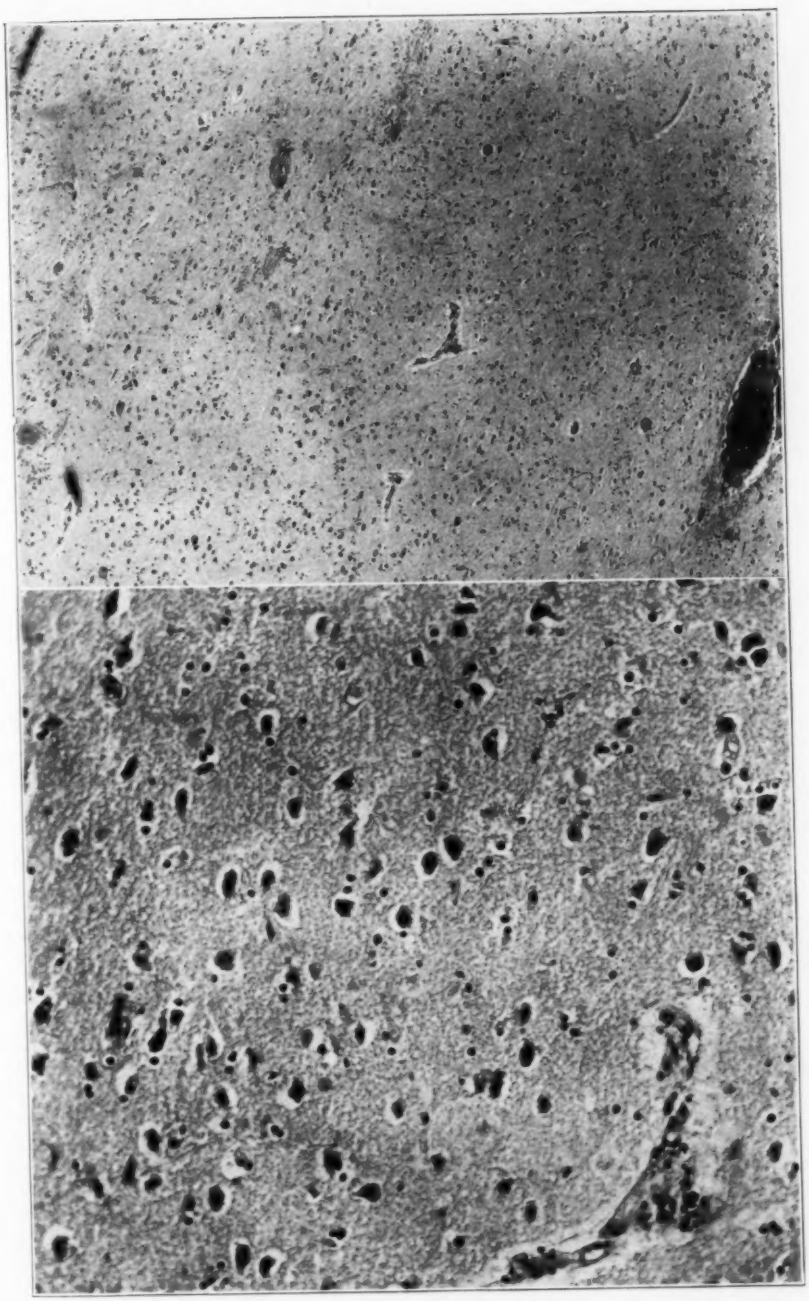
Weigert neuroglia stains in this case showed that no general neuroglia reaction was present, but around some of the larger blood vessels of the putamen there was a moderate local reaction.

The upper figure is reproduced from a photomicrograph with a magnification of about 59 diameters and shows about the usual distribution and frequency of nerve cells in the putamen.

The lower figure, which is an enlargement of the central part of the upper photograph, is reduced from a photomicrograph with a magnification of about 258 diameters. The total area of tissue taken in by this photograph is about 0.18 sq. mm., and this area contains 60 nerve cells more or less. The microscopic fields as counted throughout this investigation were about 0.25 sq. mm. in extent and were consequently larger than the area represented in this photograph.

This photograph should be compared, as to frequency of nerve cells, with the high power photograph in plate 6, Huntington's chorea; the latter is somewhat less magnified than here (about 225 diameters) and takes in a somewhat larger area of actual tissue, namely about 0.21 sq. mm. instead of 0.18 as here; still, it is roughly fair to compare the frequency of nerve cells in the two plates.

PLATE 5



Explanation of Plate 6

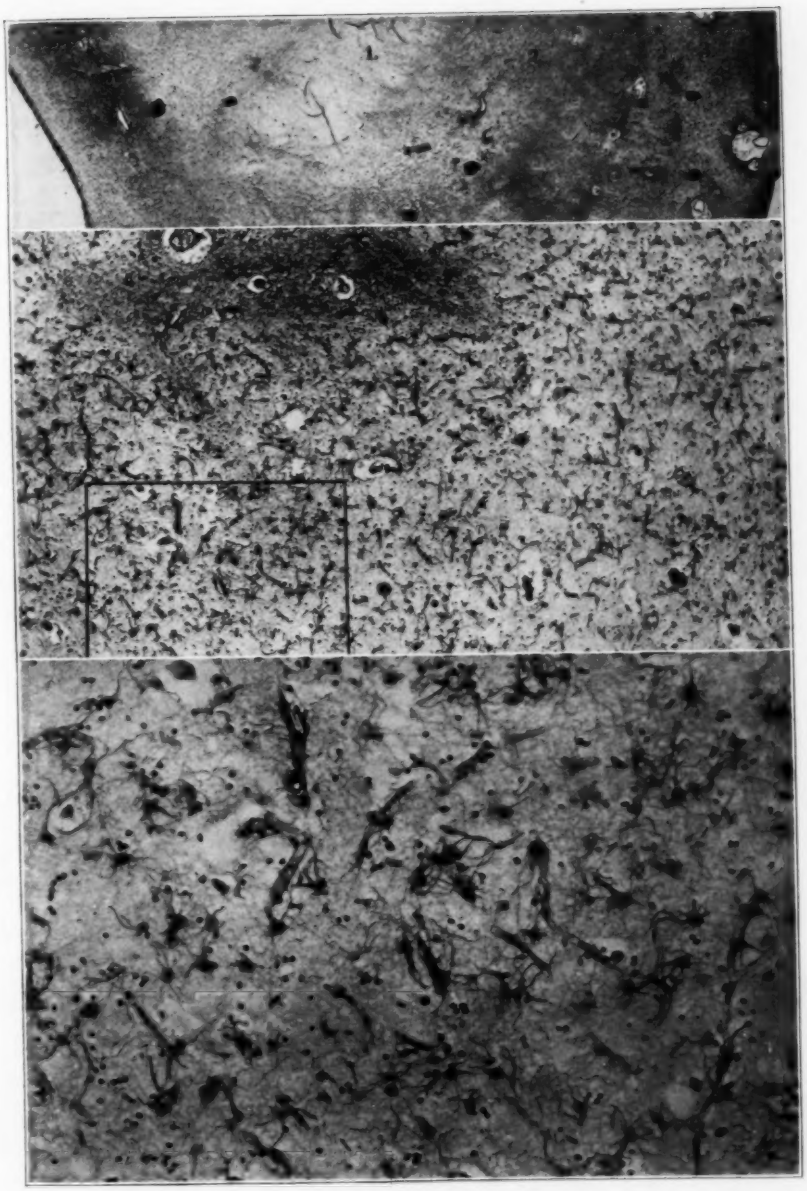
Plate 6.—Case 627: J. J., Huntington's chorea. Weigert's neuroglia stain. A section from the left corpus striatum turned so as to look like the right, illustrating especially the changes in the putamen.

The upper figure is an orientation photograph of part of the left upper striatum, cut horizontally and reduced from a photomicrograph that had been enlarged about five times. *1.* internal capsule *2,* globus pallidus; *3,* putamen. The withered up, shrunken, and darker staining parts in the putamen near the wide perivascular spaces are due chiefly to dark staining hypertrophied neuroglia fibers, as shown in the middle section of the plate, which is a photomicrograph taken from between the two ink spots just below *3.*

The middle section is reduced from a low power photomicrograph, with a magnification of about 74 diameters, of part of the area lying between these ink spots. It shows the extensive fibrous and cellular neuroglia reaction which was general in the putamen, practically amounting to a transformation of this organ into neuroglia and vascular tissue with few nerve cells remaining.

The lowest segment of the plate is reduced from a further magnification of the rectangular space marked on the segment just above. Only three recognizable nerve cells are seen in this enlargement, all on the left side. Plate 5 shows the normal number at this magnification. The tissue elements are large neuroglia nuclei and abundant coarse neuroglia fibers associated with these nuclei; numerous capillary blood vessels round which neuroglia fibers end; numerous small dark staining nuclei, many of which are regarded as neuroglia nuclei in an inactive state. Plate 5, figure *2* shows the normal frequency of nerve cells in the putamen.

PLATE 6



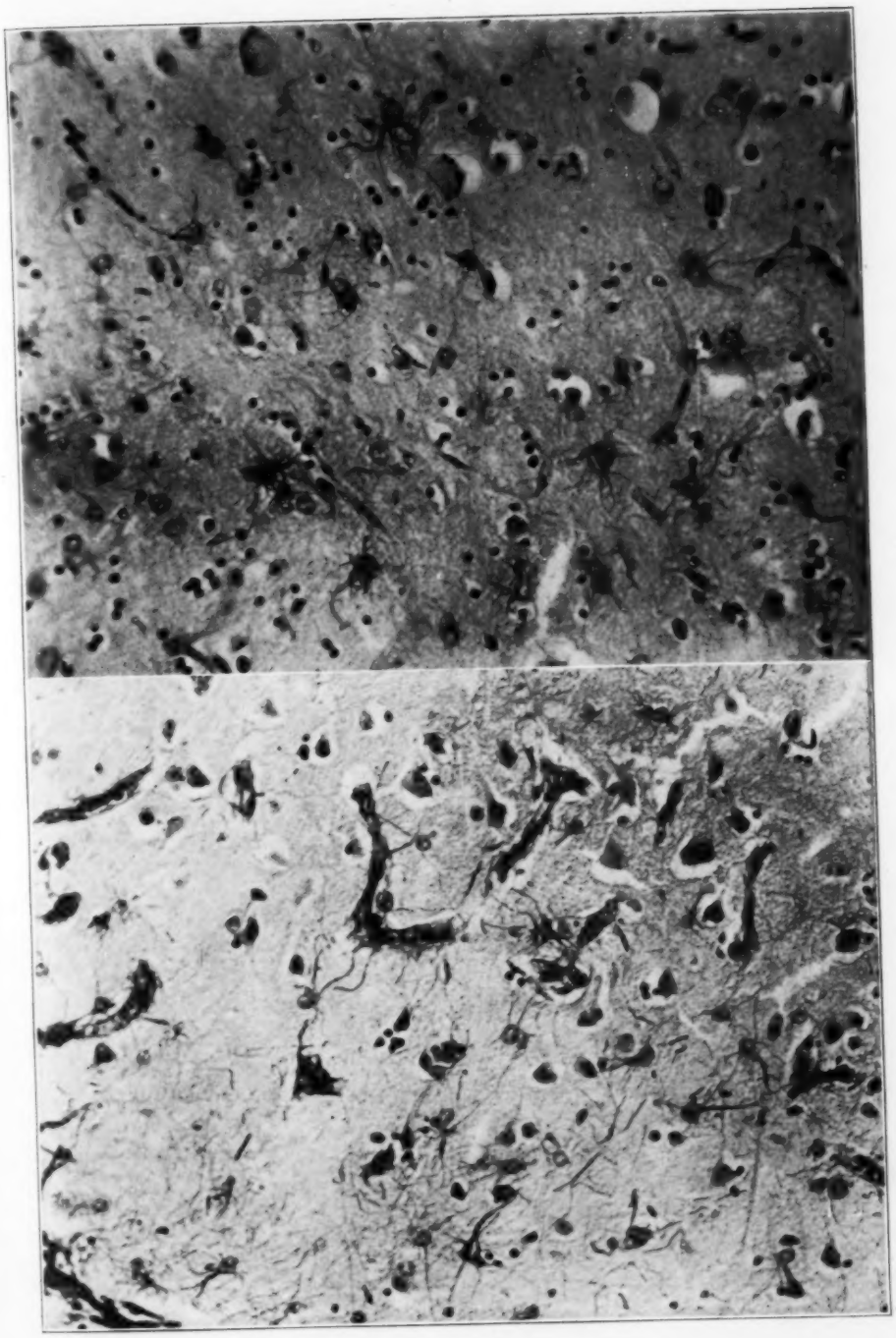
Explanation of Plate 7

Plate 7.—Comparative neuroglia reactions in Huntington's chorea and general paralysis. The upper figure was taken from the lenticular nucleus in the case of Huntington's chorea and the lower figure from the deep parolfactory area in general paralysis, to show the character and similarity of the neuroglia reaction in each. Weigert's neuroglia stain.

The upper figure, reduced from a photomicrograph with a magnification of about 312 diameters, is from the left lenticular nucleus in case 869, E. W., Huntington's chorea. Only an occasional positively identified nerve cell can be seen here. The large, active looking forms of neuroglia nuclei are often collected in twos, sometimes in threes, with coarse, pale fibrous looking processes radiating from the groups; the inactive looking forms, which are numerous, are much darker and much smaller than the former. The area of actual tissue represented is about 0.11 sq. mm. and if normal should contain about 32 nerve cells.

The lower figure reduced from a photomicrograph with a magnification of about 254 diameters, is from the deep cortex in the left parolfactory region in case 832, A. L., general paralysis. It shows, in contrast to the figure above, plainer and darker neuroglia fibers, which tend to be more uniform in caliber and to be somewhat more independent of the neuroglia cells than those shown above. There is also less tendency for the neuroglia nuclei to be bunched, while the inactive or small dark nuclei are few. Still, there is much similarity in the two reactions. The area of actual tissue included in this illustration is about 0.17 sq. mm.

PLATE 7



In the globus pallidus generally the neuroglia reaction was comparatively feeble, although it was still present, and here it was most marked in those cases showing the severest loss of nerve cells in the putamen.

The changes in the neuroglia of Huntington's chorea differ little in type from those seen in active general paralysis. In plate 7, figure 2, the two reactions are compared. I intend to present few arguments on the vexed question as to whether these neuroglia changes in Huntington's chorea are primary or secondary. My own view is that they are secondary, or rather that nervous decay and neuroglia increased activity and replacement go hand in hand. The coexistence of neuroglia that is apparently active with neuroglia that is apparently passive or inactive suggests to me, in agreement with the clinical events, that Huntington's chorea is not due to a congenital defect in the architecture of the central nervous system but is a degenerative process, in which nerve tissues are progressively disappearing, while the neuroglia is taking the usual part performed by this tissue as the nerve elements are breaking down—a part not well understood in functional details, but anatomically fairly definite.

To my mind there is no more evidence here for a primary activity of the neuroglia with secondary destruction of the parenchyma of the nerve than there is in general paralysis in which, although a similar neuroglia reaction occurs, I believe the destruction of nerve tissue to be in no sense dependent on the activity of the neuroglia tissue, but on the activity of the *Spirochaeta pallida* and its products.

The regular presence of neuroglia increase or reaction in those regions in Huntington's chorea, in which lesions of the nerve could be proved present, led to the presumption that in those parts in which such neuroglia reactions were absent no active or progressive pathologic changes were likely to be taking place. To some extent, then, the state of the neuroglia was used in an index as to whether a part was or was not abnormal.

Summary.—The corpus striatum in Huntington's chorea showed an enormous loss of nerve cells in the putamen, especially in the posterior three fourths, less loss in the anterior fourth and in the head of the caudate nucleus, and probably no loss of nerve cells in the globus pallidus, but a relative and decided increase of these. In a majority of the cases an extensive neuroglia proliferation, most marked when the nerve cells were fewest, accompanied the degenerations.

(*g*) In the nerve cells and neuroglia tissues of the red nucleus, no constant positive changes were identified in Huntington's chorea.

The corpus subthalamicum and the substantia nigra were too little studied to justify a report. The spinal cord was seldom available.

In the nerve cells and tissues of the red nucleus, no constant changes were found in Huntington's chorea. This nucleus was cut transversely in some cases, in others longitudinally. Examination of the nerve cells, which are scattered, was not wholly satisfactory and was not systematic, but it is believed that if serious defects had existed in the number or condition of these cells the control material would have made this recognizable. The condition of the neuroglia also indicated a quiescent state in this nucleus, with the exception of a rare instance or two in which a generalized neuroglia reaction was present; in such a case no greater reaction was seen in the red nucleus than elsewhere, for instance, in the external geniculate body.

The corpus subthalamicum (corpus Luysii) and the substantia nigra were too little studied to justify a report. It has been difficult to become oriented in regard to the corpus Luysii or to get a clear idea of the normal appearance and proportions of its cells and fiber systems, especially the latter, owing in part to the difficulties of uniform Weigert staining from case to case.

(*h*) In Huntington's chorea, no evidence of disease in the gray or white matter of the cerebellum or in the dentate nucleus was noticed in the ordinary routine examination (except in the case of the small cerebellum already referred to in case 699), but special attention was not given to this organ.

(*i*) In the cortex of Huntington's chorea, the nerve cells were not in obvious disorder and probably were not reduced in number, field for field: they were nearly always dark-staining, small and shrunken in appearance. The neuroglia nuclei of the cortex looked smaller, darker and more abundant than in the control cases. Neuroglia fibers often failed to stain well in the cortex, but when successfully stained they were usually most abundant at the zone of junction of gray and white matter, or in the deepest layers of the gray matter, where many of the neuroglia nuclei were large, pale and vesicular.

The white matter of the cerebral hemispheres in general was thought to be considerably more reduced in amount than the gray matter. The reasons for this conclusion have already been given.

The difficulties in dealing with the cortex of Huntington's chorea have already been discussed under methods; much further study is needed and only a few points will be discussed here. It is obvious that when a cerebral hemisphere is reduced in size or is "atrophied" at the expense of all of its parts, as seems to be the case in Huntington's chorea, the reduction in the volume of the individual convolutions, including that of the gray matter, brings those nerve cells which are still present in this gray matter nearer together than they would be if distributed through a normal amount of gray tissue. In such atrophies

of the cortex, the thickness of the gray matter from surface to depth need not be reduced, but the retraction or shrinkage in volume may take place chiefly from side to side, as seems to be the case here, while the thickness from the surface inward remains approximately the same. There was, to the measuring scale, little difference in the thickness of the gray matter in the cases of Huntington's chorea as compared with the controls but, with the microscope, the cortex in Huntington's chorea was found to be slightly less deep than in the controls.

In such an atrophied cortex, the normal number of nerve cells may be present in each microscopic field or in a succession of microscopic fields counted from the outer surface down to the marrow; the number of nerve cells in the cortex may even be increased field for field over the controls, and still an actual loss in number of nerve cells and a loss of nerve tissue may exist and does exist in the atrophied convolutions. This can be compared with the globus pallidus in Huntington's chorea in which, owing to shrinkage in size of the organ and concentration of the nerve cells into a smaller space, there is an increase per field in nerve cells, which is of course only an apparent and not a real increase in the number of these. The problem of how to determine the real state of things in the cortex, under such circumstances, has constantly baffled me; the same problem makes the atrophies in general difficult to deal with.

The fact that no loss of nerve cells was brought out in comparative counts made in the Huntington cortex does not prove, as implied above, that such loss does not exist; the contrary is more likely to be true, but I could not prove it. The cortical nerve cells in Huntington's chorea, when compared photographically with the controls, were generally darkly stained, small and looked shrunken. The shrinkage in size appeared to be mainly from side to side; the cells were not noticeably shorter than in the controls. Usually a large amount of pale yellowish material was present wtihin their cytoplasm. This resembled lipoid substance, although it failed to take the lipoid stain.

The radiating pencils of nerve fibers in the deeper parts of the cortex in the cases of Huntington's chorea often were noted as thinner, narrower and less vigorous looking than in the controls; this feature, while not always seen, was common. The marrow in the cases of Huntington's chorea seemed thinner than in the controls and seemed to contain less substance, because of the fact that it allowed more light to pass through when stained, as if it were a tissue of less density than that of the controls.

Often the smaller nerve cells of the cortical layers were so reduced in size that on general low power inspection they were hardly distinguished in size from the neuroglia; consequently their number seemed to be diminished, especially in certain layers; however, higher powers

showed that, field for field, they compared favorably in number with the controls. A search was made in the different cortical layers for defects, developmental or otherwise.[15] I was not convinced of the presence of such defects. On superficial examination it is true that some of the layers looked deficient in nerve cells, but closer attention showed this appearance to be deceptive and to be due to localized loss, but the normal cell content was present in an atrophied condition.

The neuroglia stains in the cortex of the cases of Huntington's chorea and in those of the controls were frequently unsuccessful. Such failures make it difficult to summarize the state of the neuroglia as a whole, but in some instances, especially in the deeper layers of the cortex in Huntington's chorea, there was a plain neuroglia reaction consisting in the presence of large vesicular neuroglia nuclei with, for the most part, swollen looking neuroglia fibers associated with them. Sometimes the fibers were fine and slender. The small, nonvesicular, dark-staining neuroglia nuclei usually stood out clearly in the cortex in Huntington's chorea; and they were, as a rule, more numerous than in the controls; this, as previously indicated for the corpus striatum, may mean little more than a purely mechanical bringing nearer together of the neuroglia nuclei as a result of the atrophy, or disappearance of intervening nerve material.

Comparative photographs are shown and are described in plates 9 and 10 in which the darker stained nerve cells in the cortex in the cases of Huntington's chorea are compared with the controls; these particular controls were selected to coincide with the cases of Huntington's chorea in the length of time they had remained in formaldehyde solution and with the idea of avoiding too great disparity in the ages of the patients.

DOUBTFUL CASES

[From fragmentary notes found among Dr. Dunlap's papers, it appears that he planned to discuss the doubtful cases of Huntington's chorea. A note begins, "It is beyond the scope of the present paper to discuss this group except in a general way. Each case if properly considered should be taken up individually with a short clinical résumé. This is not possible within the limits of the present article."

I have reviewed the clinical data of these doubtful cases and the descriptions written by Dr. Dunlap. The clinical picture presented by all of them was that of a chronic chorea of the Huntington type. In two cases the anamnesis was scanty, and in all of them there was either no available family history, or else one ostensibly negative for dement-

15. Kölpin: Zur pathologischen Anatomie der Huntingtonschen Chorea, J. f. Psychiat. u. Neurol. **12**:57, 1909.

Explanation of Plate 8

Plate 8.—Appearance of neuroglia stains from the lenticular nuclei in two cases of positive Huntington's chorea; Cajal's gold chloride and corrosive sublimate method for neuroglia.

Upper figure: From the left putamen in case 909, J. W. The magnification of this section was unfortunately lost, but it is probably somewhere near 300 diameters, and this figure is reproduced from approximately that magnification. The nerve cells have practically disappeared; the pale nucleus of one is seen at (*x*) near the upper left corner. The processes of the neuroglia cells are often pale and of large caliber, and extend out to the blood vessels, as at (*a*). Some of the neuroglia nuclei are large and active looking as in the cell just referred to and in others, especially the one near the center of the figure.

Lower figure: Section from the right putamen in case 911, C. B. Reduced from a photomicrograph with a magnification of about 244 diameters. No positively identified nerve cells are visible within the area photographed. All of the cells with branching processes, which resemble Golgi-impregnated nerve cells, are neuroglia elements. Nerve cells stain faintly by this method.

The whole area of tissue covered by this lower figure is approximately 0.19 sq. mm.; the size of the regular microscopic field used in the cell counts was about 0.24 sq. mm. and contained in normal cases about 70 nerve cells. This section, then, if the tissues were normal, should contain about 50 or more nerve cells.

In both of the figures — especially in the upper one (at *a*) — and on each side in the lower figure (at *b*) are seen coarse neuroglia processes extending to the walls of the capillary blood vessels and ending there.

PLATE 8

Explanation of Plate 9

Plate 9.—Appearance of sections, placed side by side in pairs, to show the condition of the cerebral cortex in Huntington's chorea and in the control cases. The sections do not reach quite to the marrow. Sims' staining method; reduced from a photomicrograph with a magnification of about 72 diameters.

The first member of each pair (*a*) is from Huntington's chorea; the second member (*b*) is from a control case. All tissues here photographed were embedded together in one block, cut together, and stained together, i. e., they received identical treatment and are strictly comparable.

The first member of the first pair (*a*) is from the left first frontal convolution in case 909, Huntington's chorea; the age of the patient is not known (table 1). (*b*) is from the same area in a control case of agitated depression, the patient being about 46.

The first member of the second pair (*a*) is from the left second frontal convolution in case 912, Huntington's chorea, the age of the patient being 57 (table 1); (*b*) is from the same area in a case of electrocution in a man, aged about 25.

In both pairs, the outer borders of the cortex have been placed in apposition as starting points. Constant features in the cortex of the cases of Huntington's chorea are shrinkage, smallness, and dark stainability of the nerve cells in all layers, while the radiating pencils of nerve fibers are often thin and delicate as in the cases here shown. The controls show plumper, larger, less darkly stained nerve cells with more clearly defined nuclei and coarser pencils of nerve fibers.

The actual number of nerve cells in the cortex in Huntington's chorea, as compared with the controls, seems approximately the same when counted with the microscope, or sometimes in Huntington's chorea the number may be actually greater field for field. Counting of nerve cells in photomicrographs of this magnification is practically impossible.

In the cortex of Huntington's chorea, increase in the apparent number of neuroglia nuclei is sometimes striking, especially under the microscope; it appears to be present in these pairs, but in the controls there are many pale neuroglia nuclei which, though visible with the microscope, are hardly brought out at all in the picture; thus, the increase of neuroglia nuclei, though frequent in the cortex of Huntington's chorea, is hardly a constant feature.

Defects in layering, if present in Huntington's chorea, were not sufficiently obvious to arrest attention.

PLATE 9

Explanation of Plate 10

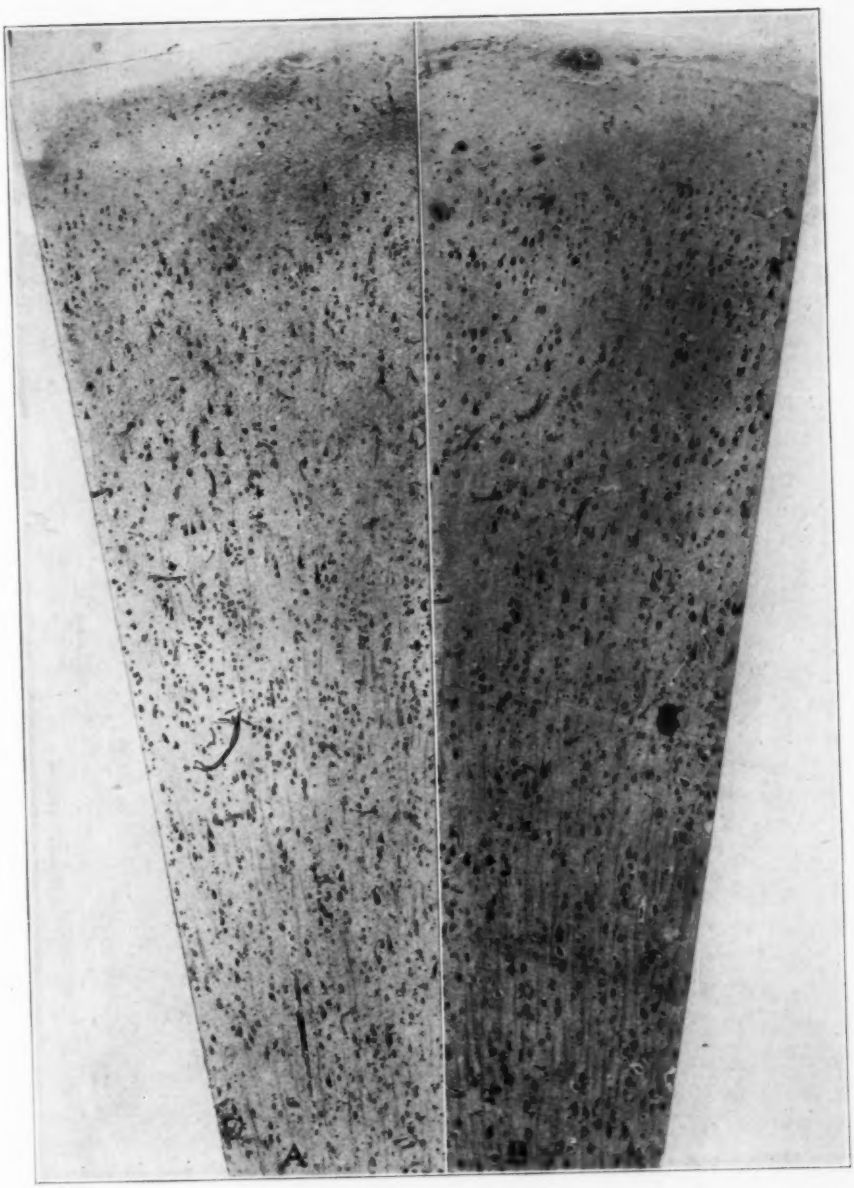
Plate 10.—Part of the cortex of the left second temporal convolution in (*a*) Huntington's chorea (from case 912, table 1) and (*b*) the same region in a control case of electrocution. Identical magnification; Sims' stain.

The frontal cortex in both of these cases is shown in plate 9, second pair; the magnification there is the same as in this illustration, namely, about 72 diameters. The plate has been reduced from that magnification.

The same features seen in the cases of Huntington's chorea of plate 9 come out clearly here, namely, small size, shrinkage, and dark stainability of nerve cells, with apparent increase of neuroglia nuclei. Owing to the small size of the nerve cells in the cases of Huntington's chorea, the number of these appears to be diminished, but actual counts with the microscope show this to be probably not true. Pencils of nerve fibers appear coarser and darker in the control case.

These two specimens, as soon as they were removed from the respective brains, were fastened together in order that they might receive identical treatment throughout; they were embedded in one block and were cut and stained as one section. The same is true of all the specimens photographed in plate 9.

PLATE 10



ing chorea. However, the trustworthiness of these "negative" histories was not great. It was Dr. Dunlap's practice to class any case as doubtful unless there was a definite, unimpeachable, positive, family history, including Huntington's chorea in one patient.

It would be incautious to attempt any discussion of the pathologic anatomy in these cases in as great detail as the author's discussion of the true cases of Huntington's chorea. Essentially, the reactions of the two groups were the same—expressed succinctly by Dr. Dunlap as: "Cerebral atrophy; reduction in size and cell content of the putamen and caudate nucleus with reduction in size, but probably no cell loss in the globus pallidus," in addition to the neuroglial changes already described.

The cell count in the basal nuclei for the cases of the doubtful group is shown in plate 4. The number of cells in each part is slightly nearer the normal than in the positive cases. Weights of the brains and measurements of the striatum for this group are shown in tables 3 and 4. Again the figures for the doubtful cases are a bit nearer the normal than are those of the cases of true Huntington's chorea.]

CONTROL CASES

[It was also apparently Dr. Dunlap's intention to devote a section of his paper to a discussion of the cases which he used as a control. They were not as a rule normal cases, but were chosen from a variety of psychotic conditions with or without atrophy of the brain. They were chosen chiefly to control the measurements of the striatum, and the cell count. Other circumstances which guided his choice are described in the early part of this paper. It seems advisable to me not to attempt a detailed discussion of these cases. The plates and tables show the contrast between this group and the two groups of chorea.]

LESIONS OF THE CORPUS STRIATUM IN OTHER CONDITIONS

In considering whether the anatomic changes in the corpus striatum as already detailed have any significance for the clinical symptoms of the disease, especially the motor symptoms, it seems well in the first place to ascertain whether symptoms similar to those of chronic progressive chorea, with the accompanying mental disorder, may be encountered with an intact corpus striatum. No such case has been met in my experience, and while in the older literature the corpus striatum often has been reported as normal in the chronic choreas, such reports were as a rule made on gross inspection. I know of no thoroughly studied cases in the literature of chronic chorea in which this organ has been found normal, but here is a field for future study.

The converse of this question at once is suggested. Do cases of profound disease of the corpus striatum occur in an otherwise intact brain in which there are no symptoms of involuntary motor disorder of choreic type? To answer this question one needs to consider the principal degenerative and destructive lesions found in this body. Under these will be included the lesions of gas poisoning, arteriosclerosis, Wilson's disease, "état marbré" as described by Cécilie Vogt, and the lesions described in paralysis agitans by Jelgersma, Hunt and others.

Gas Poisoning.—In three cases of this disease in our collection, the injurious action of the poison was by no means confined to the corpus striatum. The globus pallidus might be profoundly affected to the extent of breaking down and formation of cavities but softenings in the deep marrow of various parts of the brain were common and especially a diffuse degenerative process, characterized by the wide-spread presence of waste product cells, showed that the effects of the gas were diffuse and not sufficiently localized to make these cases suitable for a study of the function of this organ.

Arteriosclerosis.—Lesions in the corpus striatum due to arteriosclerosis are, as stated, among the commonest in pathologic conditions of the brain. It is always difficult to say, even with a complete series of sections, that no other parts of the brain are affected in this disorder, for the extraordinary difficulties in judging the presence or absence of changes, such as atrophy or failing nutrition to a part, are always present, but in many instances a focalized involvement of the striatum stands out prominently and especially that of the putamen over all other parts. Such a lesion of the striatum would at first sight justify one in expecting symptoms from this region if it is endowed with a special motor function.

On first impressions, bilateral focal lesions in the putamen of arteriosclerotic origin would seem almost ideal for bringing its functions to a test, but when the sections from such a putamen are studied with the microscope, the lesions are seen to consist of foci of more or less complete destruction, with the areas of intervening tissue essentially intact. In other words, those parts not in the zones of disintegration look well organized with the proper number and arrangement of nerve cells and with little alteration in the neuroglia. Anatomically, they look perfectly capable of carrying on whatever function they may possess. It is as if a certain amount of tissue had been scooped out of the organ in the shape of large and small holes, while the remaining tissue is left in a healthy condition. Such is not the state in Huntington's chorea in which the striatum (especially the putamen and caudate nucleus) is disorganized not in spots but as a whole; no part of it is left intact. It is a constitutional, not a local disease.

The conditions existing in the striatum in lesions of arteriosclerotic origin are closely reproduced in the experimental lesions on this organ; here spots of tissue are destroyed but the experimenter cannot accomplish the crippling of the organ as a whole as in Huntington's chorea.

Whatever may be the exceptions, the failure of these arteriosclerotic lesions as a rule to produce more than transitory symptoms referable largely or in part to neighboring structures is notorious, and their suitability for testing the functional efficiency of this organ seems questionable in view of the foregoing facts and those which follow. Moreover, if the function of the striatum is a diffuse one, as suggested by its fairly homogeneous structure, and if it does not contain "centers" for different parts of the body, the anterior part for the anterior end, the posterior for the posterior end, as suggested by some, notably by C. Vogt, much of the organ, especially on one side, might be destroyed in the arteriosclerotic manner or in the experimental manner and yet the function remain intact, just as a large amount of tissue of the kidney or liver may be lost without loss of function.

Enough doubt is thrown on the suitability of arteriosclerotic and experimental lesions as test material to make me unwilling to admit either as unequivocally suitable for testing the function of the striatum. Incidentally, these doubts suggest the reasons why both of these lesions usually do not produce any symptoms.

In plate 12 are shown the basal nuclei from two cases. Unfortunately, both are from old cases of cerebral syphilis, in which the corpora striata were bilaterally demaged by foci of destruction due to vascular disease.

Short abstracts of the clinical histories follow, showing that in neither case were there any constellations of extraordinary motor complexes (tremors, stiffness, involuntary motions) that might direct attention to the corpus striatum. It has been most difficult to find examples of extensive bilateral lesions in the corpus striatum.

Case 569—*History.*—An insurance broker of academic education, aged 48 at the time of admission to the Hudson River State Hospital, had an unimportant family history. He contracted syphilis probably at the age of 39; he was treated several years for this but had a left-sided stroke of paralysis at about 43 and was admitted to a hospital where he stayed ten days. He claimed that he was not unconscious during this attack; apparently he recovered fully and quickly from all motor symptoms, but he was considered incompetent after this, and his mind gradually became more and more feeble. His memory showed increasing loss; he did irrational things such as walking about without hat, coat or shoes in freezing weather, or passing urine in various places, with no sense of decency.

In February, 1904, he was admitted to the Hudson River State Hospital in a restless condition but was ready to talk, though he seemed somewhat irritable and wandered from the subject. He was uncertain about the day

of the month and the year, but had no delusions or hallucinations. The pupils were somewhat contracted and reacted sluggishly to light and in accommodation; smell was defective; touch was not well localized; heat was often called cold and cold hot. Otherwise the sensory tests were negative. The gait was unsteady and the balancing power poor; crude muscular strength was not mentioned. The elbow and patellar reflexes were exaggerated; the achilles reflex was present, also the plantar reflex, but there was no Babinski sign. There were marked tremors in the facial muscles and tongue and slight tremors in the fingers on extension.

At no time during the patient's subsequent stay of six years at the hospital did he fully realize his condition, but thought that his mind was not affected. He entered into the amusements of the ward in a simple-minded way, was careless in habits and showed increasing defects of memory, frequently filling in the gaps with fabrications. Judgment was markedly defective, but there was absence of any marked delusional trend or hallucinatory experience. He gradually failed physically, and toward the last of the disease he would fall while out walking and would have to be assisted to the ward.

No speech defects were mentioned in the history, and just previous to death the record states that no speech defects were present. In the initial examination, limited use of the frontalis muscle and of the corrugators was mentioned, and just before death moderate ptosis of both lids was present.

The patient died at the beginning of 1910, of acute enteritis and bronchopneumonia. Clinically, the case was regarded as one of cerebral syphilis, and autopsy confirmed this diagnosis.

Pathologic Anatomy.—The brain externally was chiefly remarkable for some evidence of old hemorrhagic pachymeningitis over the right frontal lobe and for thickening of the pia mater. The large blood vessels were diffusely thickened and showed unquestionable evidence of syphilis in the form of an exudate within their walls. The pia mater of the brain and cord was also infiltrated with characteristic cellular elements, which need not be discussed here.

On horizontal section (plate 11, figure 1), the basal nuclei on both sides showed several medium sized lacunar softenings, vascular in origin, most of which were old. Their size and position are sufficiently indicated in the figures. Neither gross nor microscopic examination of the parts in question, which were cut in partial series and stained by hematoxylin and eosin, toluidin blue and myelin sheath methods, showed on either side any essential damage in the posterior limbs of the internal capsules. Plate 12, figure 1, represents a hematoxylin and eosin stain at the level of the anterior commissure. Several lacunar softenings, however, in the deeper parts of the putamen or globus pallidus lay closely adjacent to the internal capsules without invading these to any important extent. The most that could be said was that in such places the margin of the capsule next to the softening might be somewhat paler and a little thinner than the deeper-lying parts of the capsule; the crus cerebri showed no recognizable loss of fibers and the pyramidal tracts in the spinal cord showed no positive lesions, but there was considerable exudate in the spinal pia, and the fiber stains at all levels were uneven and defective.

On the other hand, the anterior limbs of both internal capsules were partially destroyed by softenings. On the left, the head of the caudate nucleus as well was destroyed in large part by such a softening, which involved a considerable part of the anterior limb of the internal capsule though by no means all of it. On the right, a softening in the anterior end of the putamen cut into the anterior limb to a much slighter extent than on the left. At deep levels, softenings were not present either in the putamen or caudate nuclei, and the anterior

Explanation of Plate 11

Plate 11.—The upper figure, which is reduced from a photograph about three-fourths the natural diameter, shows the gross appearance in nearly horizontal section of bilateral lenticular softenings and other softenings in the basal nuclei in a case of old cerebral syphilis, 569, J. C. Stained sections from the same case, cut at a slightly different level, are shown in plate 12, upper section.

Not all parts of this brain were reduced to sections, but cuts were made sufficiently near together to indicate that no focal lesions of importance transgressed the boundaries of the large basal nuclei as here shown, if slight local involvement of the external capsule and claustrum is excepted.

The lower figure shows the left lenticular nucleus in case 369, G. M.; it is reduced from a photomicrograph with a magnification of about 288 diameters; Weigert's neuroglia stain. The clinical diagnosis was Huntington's chorea, but no history of heredity was established.

Active neuroglia reaction is obvious, as shown by the large vesicular neuroglia nuclei and coarse fibers, but nerve cells are rarely seen. The actual area of tissue included in this photograph is about 0.13 sq. mm., and should contain about thirty-five nerve cells. The smallness of this area should be borne in mind when comparing this photograph as to frequency of nerve cells or amount of neuroglia reaction with the photographs of somewhat similar magnification, as in plates 5, 6, 7 and 8.

PLATE 11

Explanation of Plate 12

Plate 12.—Bilateral focal lesions from two cases of old syphilitic disease of the arteries, located mainly in the corpora striata. Reduced from a photomicrograph with a magnification of about 1½ diameters. Hematoxylin and eosin stains. The level of the sections is about the same as that shown in the figures of plate 2. No clinical syndrome, such as is claimed by Wilson for the corpus striatum, was present. In the right half of the upper figure (case 569), there are two plain softenings with loss of substances in the putamen; one is near the middle of the lateral part; the other is a long interrupted softening in the posterior end. There is also a softening in the anterior part of the right optic thalamus.

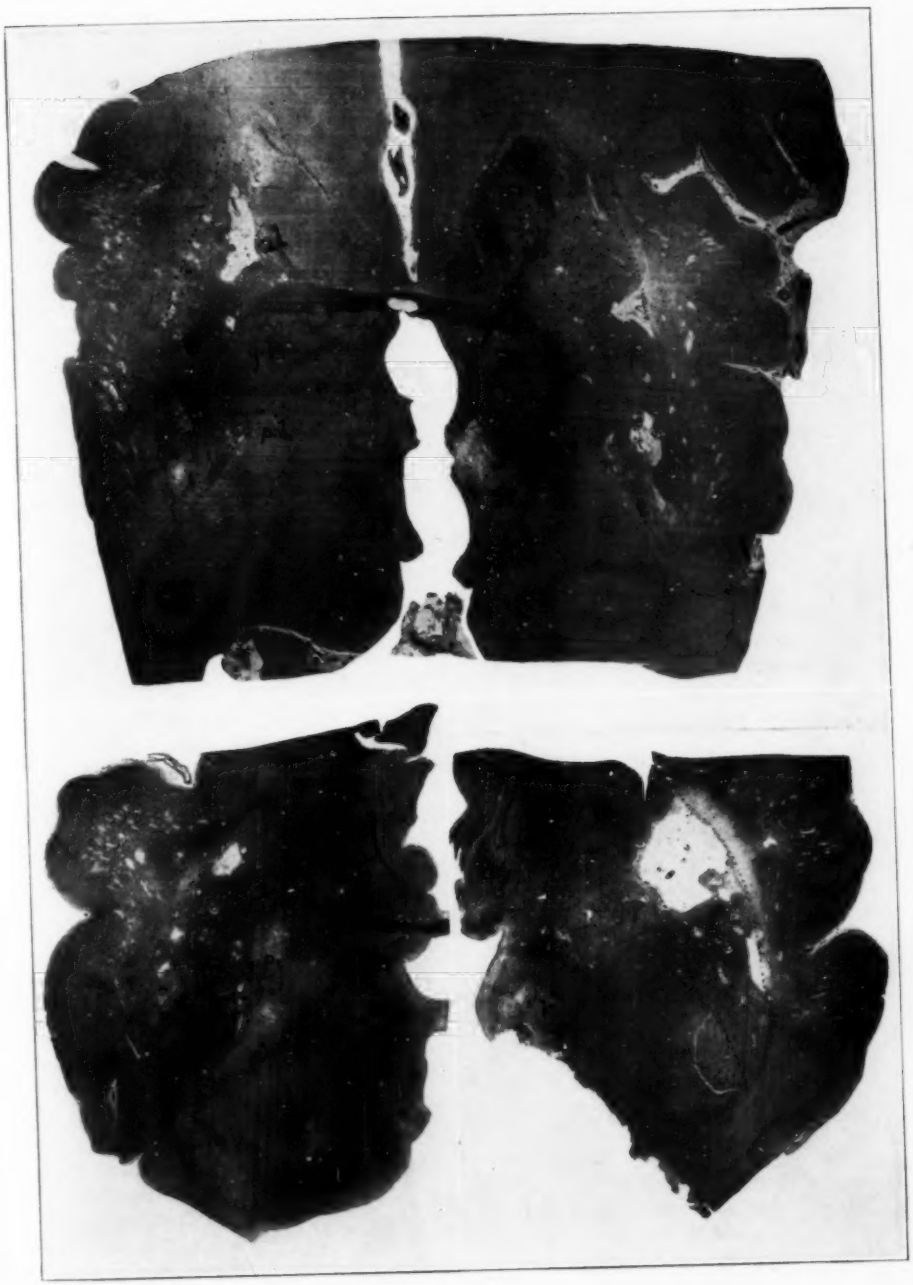
On the left, the anterior and larger of these cuts into the anterior limb of the internal capsule, and is situated not at the margin but in the deeper parts of the putamen. The posterior softening is small, but is roughly symmetrical in position to that on the right.

Landmarks are rather hard to see, and dotted lines have been added to indicate boundaries partially. The anterior commissure, *a.c.*, joining the two halves of the section, is plain, as are the anterior limbs, *a.l.*, of the internal capsules; the posterior limbs, *p.l.*, are less plain but are indicated by dots. On each side are seen the convolutions of the island of Reil.

The lower figure (case 729) shows sections cut at about the same general level as in the upper figure, at least on the left side. There are three small pits of softening along the external margin of the left putamen; one pale area of partial softening shows near the middle of the globus pallidus, and there is a slight nick in the lateral edge of the posterior limb of the internal capsule, about 1 cm. back of the knee; this nick did only slight damage to the capsule at this level. On the right, in about the second quarter of the putamen, is a large cavity due to softening, and there is a smaller one about 1 cm. further back. The larger softening affects the putamen and external capsule almost exclusively, the globus pallidus being only superficially invaded at the outer edge. The pale staining lateral margin of this softening is mostly in the external capsule, and the claustrum is only slightly affected. The smaller softening takes in the outer edge of the putamen and the inner edge of the external capsule. At other levels in the basal nuclei, these relations were much changed, but considerable inroads were made into the substance of the putamina of both corpora striata by lacunar foci of softening, which lay at different levels. In neither of the cases was the posterior limb of the internal capsule seriously affected, not as much so as in one of Wilson's cases.

Many objections from Wilson's point of view may be brought against the use of these cases of lenticular softening as material with which to test the functional rôle of the corpus striatum. Neither case is pure; both are from old syphilitic patients with diffuse disease of the cortex and meninges; in neither are the obvious focal lesions absolutely limited to the corpus striatum. A further serious objection to using these cases for such a purpose — an objection that applies to most if not all arteriosclerotic material — is that the tissues in those parts of the striatum not softened look approximately normal both as to frequency of nerve cells and often as to general neuroglia content; the disease process in arteriosclerotic conditions generally, whether of syphilitic etiology or not, does not produce disintegration or disease of the organ as a whole, but the damage is, according to the author's experience, largely focal or insular in character, while much tissue, which looks healthy and adequate for function, is left intact. Such is obviously not the case in Wilson's disease, nor in advanced Huntington's chorea, in which the integrity of the whole putamen as an organized tissue is essentially destroyed on both sides; scattered individual elements of normal appearances may persist, however, in this fundamentally altered and disorganized tissue.

PLATE 12



limbs of both capsules were preserved. Outside of the areas of softening described, the organization and nerve cell content of the corpora striata were regarded as normal. By far the greater part of the organs to all appearances, was thus preserved intact and in a state of functional efficiency.

Comment.—In regard to the view of C. Vogt and others concerning the functions of the striatum in the mechanism of speech, it may be noted that notwithstanding these bilateral focal lesions in the caudate nuclei, putamen and in both anterior limbs of the capsules, the patient, according to the record, showed no speech defect.

[Case 729.—*History.*—A locomotive engineer, aged 53, was admitted to the Manhattan State Hospital, March 17, 1909. The family history, so far as mental or nervous disease was concerned, was negative for the two preceding generations. At about the age of 23 he contracted syphilis, and received antisyphilitic treatment for two years. He married shortly after this; his wife bore two children, the third pregnancy ending in a miscarriage. He drank heavily, so much so that his wife left him nine years before his death. In the same year (1902), he suddenly fell down in the street; he was not unconscious or paralyzed, but the physician who saw him then said that his heart was affected. Soon after this, he had a similar attack. From this time on, he no longer worked as an engineer but undertook various poorly paying simple jobs.

For about five months previous to admission to the hospital, he had been engaging in conversations with imaginary persons. He had been confused and dull, wandering about aimlessly "hunting for money," once without his clothes. On admission, he was dull and confused and fabricated freely. Though quiet and uninterested, he was happy. He stated that he came to the hospital "to see a doctor," and knew of no other explanation of his presence there. He was disoriented and mistook dates. Grasp and calculation were defective.

He complained of severe headaches once or twice a week, and at times of dizziness, both symptoms being more troublesome at night. He did not name the solutions used for testing the olfactory sense. The pupils were unequal and irregular but preserved reactions to both light and accomodation. No hemianopia was present. The face on the right side was flattened and weak. The tongue protruded to the right. The right arm and leg were weaker than the left, and the deep reflexes on this side were exaggerated. The superficial reflexes were active, and there was no Babinski sign. Sensation was not altered. There was no speech defect on admission, but writing was tremulous and frequently illegible. At a later date, speech was said to be slurring. The peripheral vessels were thickened; the systolic blood pressure was 210. The Wassermann reaction was positive in the blood serum and in the spinal fluid, with a lymphocytosis in the spinal fluid of from 10 to 12 cells.

During his stay in the hospital, the mental picture was not altered. He felt happy, was apathetic, confused and disoriented, and memory and retention were extremely poor. Physically, an increased slurring in sppech was the only perceptible change. He died on Dec. 24, 1911, the clinical diagnosis being cerebral syphilis and pulmonary edema. Both of these diagnoses were confirmed by the autopsy.

Anatomic Observations.—The brain externally showed a moderately thickened and gray pia, especially over the convexity of the cerebrum. The vessels were thickened but showed little atheroma. Microscopically, a girdling endarteritis of well organized tissue was seen, with little degenerative change, and in the sheaths of some of the vessels was a well marked lymphoid infiltration.

No focal lesions were to be seen on the surfaces of the uncut brain except in the right hemisphere of the cerebellum. This hemisphere was smaller and softer than the left and its surface was uneven, showing small pits to which the blood vessels seemed in part to converge. The blood vessels of this side looked smaller, were more thickened and contained more blood. There were a few elevations on the floor of the fourth ventricle. The cranial nerves were not unusual. Separating the cerebral hemispheres revealed some atrophy of the mesial aspect of the frontal lobe and a few scattered whitish granulations in the third ventricle.

Horizontal sections were made in each hemisphere at the level of the middle and anterior commissures. On the right, this showed an extensive softening in the putamen which ran from near the anterior limb of the internal capsule backward along the border of the external capsule. A smaller cavity of the same sort was seen about 1 cm. behind this. The microscope showed that the larger softening affected the putamen and external capsule almost exclusively, the globus pallidus being only superficially invaded at the outer edge. The claustrum was only slightly affected. The smaller softening took in the outer edge of the putamen and the inner edge of the external capsule. At a cut 1 cm. above this level, made at about the junction of the corona radiata and the internal capsule, a lesion was seen cutting extensively into the anterior part of the internal capsule and invading as well the head of the caudate nucleus and probably the anterior third of the corpus callosum.

The horizontal cut through the middle and anterior commissures on the left showed a small pit of softening along the external margin of the putamen. About 8 mm. behind the knee of the internal capsule was a ragged patch of partial softening apparently of the whole internal capsule. A section 1 cm. above this level showed the lesion destroying the anterior limb of the internal capsule and involving slightly the caudate nucleus and the corpus callosum. This lesion seemed to be continuous with the one at the lower level. At other horizontal levels, the relation of the lesion was somewhat different. At the level shown in plate 12, figure 2, softenings in the deeper part of the putamen were seen, as well as a small one in the globus pallidus.

The posterior limb of the internal capsule was not seriously affected.

A detailed description of this level will be found in the legend opposite plate 12, in which the significance of these observations is discussed.

This summary of the case is compiled from the notes made by Dr. Dunlap, and from the case record].

These arteriosclerotic cases represent fairly the usual run of symptom-free bilateral lesions in the corpus striatum that might be used in the discussion of Wilson's claims; they also agree in lack of symptoms with the experimental lesions in the striatum of animals (Wilson, Probst [16] and others) which cause no recognizable disorder in function even when of large size. Focal lesions such as these are probably unsuitable for bringing to a test the function of the corpus striatum as an organ. The putamen and the caudate nuclei are homogeneous in structure, and all of the bilateral arteriosclerotic lesions I have examined by means of sections leave much of this homogeneous material quite intact. There-

16. Probst: Experimentelle Untersuchungen ueber die Anat. und Physiol. des Sehhügels, Monatschr. f. Psychiat. **7**:387, 1900.

fore it seems to me that the most suitable cases on which to test the functions of this organ are not the arteriosclerotic or the experimental lesions but are those lesions which are in the first place selective, confined to the parenchymatous tissues of the organ, and in the second place those which are not focal but destroy the integrity of the organ or its parts as such throughout. The only case records I have been able to find personally or by appeal to the New York State Hospital system or in the literature, which approach these desiderata of selective organ lesions, are those of Huntington's chorea, C. Vogt's cases of état marbré, and Wilson's cases of so-called progressive lenticular degeneration.

In Huntington's chorea and in all of the cases reported by the authors just referred to, so far as I am able to judge, the corpus striatum is profoundly altered, as an organ, and not in the spotty or patchy way seen, for example, in arteriosclerosis, although certain parts may be, and are, more involved than others.

The main difficulties begin when one asks: Is the corpus striatum in the organic diseases described the only part affected, and can the functional disorders and clinical symptoms be referred solely to this region? Wilson and C. Vogt, as far as their examinations went, found no significant disease process outside of the basal nuclei in their cases, but one feels the need in both instances of a much more searching study in other parts of the brain than they have reported, especially perhaps in the cortex. In Huntington's chorea, at least, degenerative changes in the cortex are not hard to find and it can be stated that they are regularly present. How important they are for the characteristic motor phenomena of this disease is another question, and one hard to answer.

It is evident, with much more thorough work needed in the histologic study of the regions indicated, that there is not enough accurate data on the anatomic side even to begin a real analysis of the claim that the corpus striatum is an organ exerting a special influence on motion, but the question will have to be approached from another side, with a formulation about as follows: Are there any observed or reported cases of disease and disorganization of the corpus striatum, as an organ, in which the patients gave no evidence of motor disorders of any kind? If motor disturbances were regularly present in lesions of the striatum of this kind were they of a type more or less similar to one another?

To state my own experience first, I can say that I have not yet found a case in which the corpus striatum was disorganized as an organ which did not at the same time have a history of motor defects of an uncontrolled character. With this point in view, I have been through much material not reported in this paper, looking for lesions in the striatum which would destroy it as an organ, and I have not found any such case outside of Huntington's chorea, except one case showing such tremen-

dous fresh parenchymatous degeneration everywhere, in the pyramidal tract, cerebellar tract, fillet and other areas, including the striatum, that it could not be used to test the functions of this organ. On the other hand, I have found the corpus striatum profoundly altered in every case of positive Huntington's chorea in which I have made an examination; also, as a rule, it has been profoundly altered in the group of choreas lacking a positive heredity or in which the heredity was unknown, some of which at least were probably true Huntington's chorea. My experience does not include Sydenham's chorea, but is limited to the chronic choreas.

In the literature, moreover, I have so far not encountered any cases of bilateral disorganization of the corpus striatum, as an organ, which did not at the same time show involuntary muscular phenomena in the nature of chorea, athetosis or tremors as in the Wilson type of cases.

On the other hand, the literature teems with reports of cases of involuntary muscular activity in which at auptosy no lesions were reported in the corpus striatum; but in the vast majority of these cases, examination of the striatum was most superficial and was not in the least way adequate to detect disease of the kind under consideration, even if present; consequently, this aspect of the question must be left to the future.

It is only necessary to recall the decades during which the grossly recognizable defects in the corpus striatum of Huntington's chorea have gone undetected to realize how carelessly examinations in this region have been made in the past. Hemichoreas have been attributed to lesions in various regions, particularly to thalamic lesions and sometimes to lesions in the striatum, probably for the reason that such lesions were grossly apparent and often no sufficient attempt was made to see whether a given lesion was the only one that might give rise to symptoms. No real attempt was made to examine further the condition of the corpus striatum or that of the other basal nuclei.

For the solution of this problem, then, all such poorly observed cases must be discarded, which means that most of the early literature has to be disregarded, owing to the superficiality of the observation in the basal nuclei and owing especially to the lack of microscopic-investigation of these regions. Even in serial sections stained by Weigert's method, lesions of the type I am dealing with might easily be overlooked. The study is essentially a study of the tissues, including all of the elements, and is not merely a study in myelin sheaths.

The following facts are the most significant: Whenever the corpus striatum has been found disorganized as an organ on both sides, although the pyramidal pathways were apparently intact, involuntary movements of choreiform athetoid or tremor-like character (and not infrequently mixtures of these) have coexisted. So far I have not been able to find

exceptions to this statement, as the only bilateral lesions that I know of the character described occur only in Huntington's chorea, in the état marbré of C. Vogt and in Wilson's disease, while paralysis agitans is still *sub judice*. On the other hand one cannot say by any means that whenever involuntary motions of choreiform athetoid or tremor-like character have been observed, autopsy has shown destructive lesions in the corpus striatum.

I have looked in vain among my own cases and in the literature for true disorganizing lesions in the corpus striatum which do not give rise to motor symptom lesions or other symptoms, but I have not found them. Focal lesions in these organs are among the commonest lesions of the brain, but as already suggested such lesions (and one might here include experimental lesions) are more like punch holes in the organ, while much of the parenchymatous tissue still looks well organized and healthy under the microscope. For all I know, this remaining healthy tissue may be fully adequate for the amount of function this organ exercises in man. The absence of definite motor symptoms in arteriosclerotic lesions of the corpus striatum and in experimental lesions then suggested that a part of this more or less homogeneous body may carry out the function of the whole, as part of the kidney or part of the thyroid gland may be ample for all needs. These lesions also carry another suggestion, namely, that the corpus striatum has no influence whatever in motion and that when motor disorders coexist with true organic lesions of this organ, the two are not connected with one another but are independent phenomena.

This of course assumes that whatever motor function the striatum may still have in man is a diffuse function, and that the different parts of the animal body are not represented in this organ by special mechanisms or nuclei of which, anatomically at least, there is little evidence. C. Vogt brings some evidence to bear on this point by reporting lesions (état marbré) that affected chiefly the anterior part of the striatum and were associated with motor symptoms in the upper part of the body—a pseudobulbar syndrome; while with lesions (état marbré) limited to the posterior parts of the striatum, the upper part of the body was free from symptoms while the lower part was affected. The number of well observed cases in this respect is, however, too small to establish such a relationship safely, or to prove the existence in the striatum of special nuclei presiding over special parts of the body in the face of considerable evidence, derived from arteriosclerotic or other focal lesions, which supports a contrary view.

[Here the manuscript breaks off, and a few notes found suggest that a discussion of Wilson's progressive lenticular degeneration, C. Vogt's état marbré, and the changes in the globus pallidus described by Hunt

for paralysis agitans was to follow. It would be hazardous to attempt to state the reasons that led to Dr. Dunlap's views on Wilson's or Vogt's work. He believed, as he states later on in the paper, that in both it was not completely and unimpeachably proved that the striatum alone was affected. He was, however, open to conviction on this point, believing that future work might be more conclusive, particularly that the determination of the cerebellar-cerebral weight ratio might help to prove the presence or absence of cerebral atrophy. Unfortunately, he had no opportunity for the personal study of a case of either type.

He was skeptical of the validity of the conclusions arrived at by Hunt in regard to pallidal degeneration in Parkinson's disease. A fragmentary note states:]

In paralysis agitans, on the other hand, while there is possibly some decrease in the size of the lenticular nucleus (though I have not been able to verify this), there has been in all cases at my disposal a thinning and paleness in the fibers of the ansa lenticularis, as has been shown by Jelgersma and more recently by J. Ramsay Hunt. Some degeneration of the nerve cells in the globus pallidus and some diminution in their number have also been found by Hunt. So far, in our material I have not been able to get convincing evidence of such actual loss in the number of nerve cells in the globus pallidus in paralysis agitans (table 5). Except in the ansa lenticularis, in which loss of fibers seems to exist, the lesions, if present, do not reach the dignity of major lesions, but stand as uncertainties or possibilities, too unclear to reckon with in a study such as this, whose scope as stated takes in mainly the grosser traits of cerebral pathologic, change such traits as any one can see. The nerve cells in the globus pallidus of paralysis agitans seem about as numerous as in the control cases, and it is these cells which give origin to those ansa fibers which pass in an outgoing direction from the globus pallidus to the thalamus to end mainly in the hypothalamus. Fibers passing into the corpus striatum from without are also present in the ansa lenticularis, but the number of these incoming fibers is thought to be smaller than the number of those which are outgoing. It has been assumed, though not proved, that in paralysis agitans the outgoing fibers whose cells of origin are in the globus pallidus are the ones degenerated. I was not fully convinced that such was the case, as the loss in stained fibers was well marked, while the cell count in the pallidus was about up to the average.

POSITIVE CASES OF HUNTINGTON'S CHOREA

CASE SUMMARIES

CASE 34.—M. W., a woman, aged 30, was admitted to the Rochester State Hospital, Oct. 17, 1902. The maternal grandfather died in an asylum of Huntington's chorea; the mother, a maternal aunt and a brother were similarly affected. The choreic movements began six years before admission and became progressively worse. She became depressed and suicidal one year before admission, and mumbled to herself. Choreic movements were present in all groups of muscles, with a peculiar tic of the glottis illustrated by the syllable "cluck, cluck"; the movement was less marked during voluntary activity. She refused food, lost interest in the surroundings, and developed pain in the head and difficulty in swallowing. She died Dec. 7, 1903. The autopsy was performed three hours post mortem.

Case 67.—M. P., a woman, aged 35, was admitted to the Rochester State Hospital on Dec. 15, 1903. The paternal grandfather, father, two paternal aunts, two paternal uncles and two brothers had had chorea and mental symptoms. When in her teens, she was irritable and impulsive; she was in the State Industrial School for some petty offense, and three times threatened suicide with laudanum. She had had "hysterical" attacks all her life, but was a fair domestic servant. A year before admission she became depressed over a sister's death; her hands began jerking and she felt "dizzy in the legs" when working; she took laudanum because offended at something said to her. On admission she was restless, changed position frequently, complained of feeling dizzy, and it was said she walked like a drunken man at times. Choreic motions were seen in the toes and fingers, in the latter a slow abducting movement of the first finger away from the middle finger. The rest of the body was affected markedly only two weeks preceding death. Mentally she was depressed and irritable. She committed suicide by using carbolic acid, May 7, 1904. An autopsy was performed by the coroner.

Case 68.—J. D., a street car conductor, aged 32, was admitted to the Long Island State Hospital, Dec. 17, 1900. The father and one sister showed chorea and mental symptoms. The past history was unknown. When admitted he talked in an irrelevant manner and was in continuous choreic motion. He demanded his release and stated that he heard voices. He wandered about aimlessly and thought he was being poisoned. For a year and a half prior to death he could not feed himself, became emaciated, bed-ridden, and died on May 5, 1904, from exhaustion.

Case 627.—J. J., the wife of a railroad man, was aged 38 when admitted to the Middletown State Hospital on Aug. 14, 1905. The father had had the same disease as she and died in a Washington asylum. The mother had had a marked tremor all over the body for many years before death. She was said to have been healthy till marriage; became ill after the death of her husband and of a newborn baby. She then went to an almshouse. Just previous to this, in August 1903, she became violent, muttered to herself, answered questions irrelevantly, and at the almshouse broke the windows of her room and threatened to kill the attendants. On admission to Middletown, she showed marked choreic movements of the head and face muscles, and of the arms, occasionally also of the legs. She had an articulation difficulty, was disoriented as to time, and later developed unsteady gait; she stumbled and fell frequently, hoarded scraps of rag and paper which she pinned to her dress and became violent at times. When angry, articulation was clearer. In 1909, she failed physically, became weaker, developed bedsores and furuncles, and was bed-ridden. She regurgitated food through the nose. She died Sept. 19, 1910, of edema of the lungs. An autopsy was performed nineteen hours post mortem.

Case 699.—H. W., a laborer, aged 42 (seven and one-half weeks in the hospital) was admitted to the Hudson River State Hospital on June 28, 1911, from jail. The father's father had had chorea, the father's mother died of nervousness, the father died in the almshouse with chorea at 50, the mother had no nervous disease, but three of the father's brothers had chorea and one of the father's uncles had chorea and killed himself. The patient's brother was insane and had chorea; another brother was likewise, and hanged himself. A third brother has chorea, two sisters are both inferior, and one has chorea. The father of the patient's wife probably had chorea, the patient's wife was nervous and showed chorea at times, but a son (at the age of 22) appeared normal. The patient was always inferior, had difficulty in studying and learning; he married a first cousin; they could not get along together. The patient was a good farm laborer until four

years before admission. Mental symptoms were first noticed on April 19, 1911, when he became restless and talkative, thought his sheep and dogs were in the trees, and thought the dogs were after him. He became incoherent, could not care for himself and was taken to jail. On admission he was obedient, but later resistant and difficult to manage, objecting to going to meals, and then to being taken away from the table. He tried to hide, was restless at night, and wandered about the ward. Aug. 20, 1911, he was assisted in dressing and sat down; in less than half an hour he died without moving from that position. The speech was difficult to understand; there was apparent difficulty in forming words and jerky speech. He said he tried to drown himself because he was tired of life. Ghosts and voices bothered him at night. Although he said they were imaginations they bothered him just the same. He was disoriented, with poor grasp on the past, and could give no dates, not even the date of his birth or other important events in his life; he could not write and said he was half crazy. He was fairly developed; hearing, sight, taste and smell were defective. There were marked incoordination; absence of abdominal and cremasteric reflexes; atrophy of the left testicle; choreic movement of the whole body; slow speech and mental activity; the deep reflexes were normal.

CASE 702.—E. G., a farmer, aged 75, was admitted to the Gowanda State Hospital, Aug. 17, 1909. The mother had chorea and progressive dementia at 40; the brother had had the same since 42; choreiform movements at middle age have been common for generations on the mother's side. The patient was bright as a boy, normal till middle life, then shrugged his shoulders, moved this eyes and made slight movements with his head. Later the entire body became affected. Two years before admission there appeared delusions of power and wealth, and persecutory ideas. He grew filthy, demented and was committed. He was small, in poor condition, with marked intention tremor and choreic movements beginning in the abdomen, extending first to the upper extremities and then to the lower limbs. They were almost continuous while he was awake, but absent in sleep; the pupils were normal; the reflexes were increased; there were poor coordination, a mitral lesion, general ateriosclerosis and nephritis. He was disoriented and had delusions of persecution; speech was mumbling and incoherent; he was filthy in habits and had no insight; he appeared demented and lost ground steadily. Choreic movements became so marked that he could not stand. Swallowing became difficult; the sphincters were not under control. Death occurred Jan. 29, 1911. An autopsy was performed three hours post mortem and revealed interstitial nephritis, and arteriosclerosis.

CASE 744 (Combined general paralysis and Huntington's chorea).—I. T., a man, aged 46 at death, was admitted to the St. Lawrence State Hospital, July 4, 1907; the mother and six of her sisters and five of her brothers all had Huntington's chorea. The patient's brother has Huntington's chorea and one sister died of it. He never attended school, was in the poor house, developed Huntington's chorea at 38, and a psychosis began about two and one half years later with wandering around, instability, irritability, threats to kill and incoherent talk. He tried to kill imaginary flies and mosquitos, while stating that he must get an ax and kill someone. He was well nourished; the pupils were normal; he had rather poor balancing power and an unsteady gait. There were choreic movements of the arms, head and legs; all reflexes were increased; the tongue was slightly tremulous. He was quiet, and his grasp on admission was quite clear for simple questions; also he was well oriented except for time, which was poor. He gave a fair account of his life except for dates; he had no school knowledge. He denied all delusions; said he came to get cured of "St. Nancy's Dance but his

mind was all right." No subsequent notes were made until January, 1910; he was then very unsteady and grew untidy, spilled food, etc. In November, 1910, speech was very thick; he could not dress himself and he realized his condition. The subsequent history is one of deterioration. By Oct. 7, 1911, he had become unintelligible. The chorea involved the whole muscular system. On Feb. 19, 1912, he became unconscious with rapid failure and death occurred Feb. 23, 1912. He was well nourished; the cerebrospinal fluid was increased; the basal vessels were slightly atheromatous; granulations were present in the fourth ventricle; the weight of the brain was 1,235 Gm. There was a small ulcer with an organized clot just below the aortic arch. The other organs were essentially normal.

Case 781.—B. V. W., a woman, was admitted to the Willard State Hospital, in October, 1910, at 48; the mother's father, uncle and five brothers and sisters had chorea. She had always been nervous. Chorea began at 42; five years later, and five months before admission, the psychosis appeared. She was despondent, thought her husband was unfaithful and tried to have him arrested. On admission she was oriented, understood the situation, gave a fair history and had fair retention and insight, except that she stuck to the infidelity of her husband. She had moderate chorea, increase of deep reflexes, left pupil larger than the right; the right grasp was rather weak, otherwise there was fair muscular strength; memory was good except for periods of time and dates, but she had trouble in calculation. She remembered daily occurrences. In retention tests she did poorly. She did not grasp simple stories. The most marked thing seemed to be the difficulty in mental exertion such as calculation, fixing dates and giving attention to a story, but the actual data of her life were well reproduced. She remained thus until January, 1913, when she showed pulmonary tuberculosis and died April 15, 1913. Choreic movements continued to within an hour or two of death. An autopsy was performed twenty-two hours post-mortem and revealed emaciation, tuberculosis in both lungs, weight 86 pounds, excess of cerebrospinal fluid. The clinical diagnosis was: Huntington's chorea; tuberculosis of both lungs.

Case 869.—E. W., a farmer, aged 56, was admitted to the Willard State Hospital, March 15, 1906. The maternal grandmother, two maternal aunts, the mother and two brothers were afflicted with chorea. He had an attack of chorea at the age of 9, but was not troubled after that till he was 42, when he began making twitching movements. The mental symptoms started in 1898, when he was 49. While working in a field with his son, he suddenly ran away and hid and told the neighbors his son wanted to murder him. Other attacks of this sort occurred at intervals and lasted from one to seven days. On admission he showed constant small choreic movements and unsteady gait. The movements disappeared in sleep or on voluntary exertion. Mentally, he was irritable and depressed; he was oriented but grasp on the immediate past was poor. He could not remember objects shown him after a few minutes. He became progressively more irritable, inclined to annoy other patients, and finally untidy, simple, and childish in manner. He died Nov. 4, 1914, of typhoid fever. Autopsy showed ulcers in the ileum, enlarged mesenteric nodes, arteriosclerosis and chronic interstitial nephritis.

Case 892.—L. Du., a woman, was 52 when admitted to Central Islip State Hospital, March 27, 1908. Her father "would throw his arms." A brother was J. M., case 912. The past history is unknown. On admission she was euphoric with persecutory ideas, and ideas of possessing great wealth; she made numerous date discrepancies, talked in a rambling manner, laughed in a silly fashion and

gave the general impression of a dementing general paralysis. Physically, she showed jerky, explosive, interrupted speech, and constant jerkings of the arms, legs and body, sometimes even in sleep. She deteriorated mentally, lost weight, and died at the Gowanda State Hospital of bronchopneumonia, April 29, 1915. The brain showed an acute meningitis.

CASE 909.—J. W., the anamnesis was not found in the case record. The heredity card revealed that the paternal grandmother, a paternal uncle, and the father had had Huntington's chorea.

CASE 911.—C. B., a bad-tempered domestic, aged 32, was admitted from the County Hospital to the Middletown State Hospital, Feb. 15, 1907; she died Jan. 28, 1916, at the age of 41. The maternal grandmother, and the mother, who died at about 35, had "St. Vitus' Dance" at the end of life; a sister also died after having had the same chorea as the patient. The sister was an adopted child. At 12 years of age the patient was very anemic, irritable and inclined to get in a passion. She married at 17 and had two children, one of whom died in infancy. She had typhoid fever at 29, which lasted about five months; during convalescence the head twitched, and about the same time twitching began in the arms and legs. From that time the chorea became progressively more marked. At 31, ten years before death, she went to an almshouse, but was so unmanageable that she was committed. She was six months pregnant on admission; she was correctly oriented and had fair memory. Irritability and conflict with other patients were the main traits; when not angry she was not vicious. She tried to walk but was too awkward and lacking in muscular control. Unsteadiness gradually increased; choreic movements were constant and distressing. Up to ten months before death she was oriented and kept up interest in people and things, but speech became so bad that it was difficult to understand her. Seven days before death, after a fall and a wound "above the nape of the neck," an apparent convulsion, probably with loss of consciousness, was followed by a milder one in which choreic movements ceased; they gradually recurred after consciousness returned, but three more convulsions occurred that same day. The day before death the temperature suddenly went above 104 F. An epidemic of grippe was prevalent at the time and her illness seemed like that of others affected. She was alert and restless twenty minutes before death, which came unexpectedly Jan. 28, 1916, when she was found dead. An autopsy performed thirty-two hours after death revealed: emaciation; no bed sore; brain small, but not weighed, with normal external appearance; the lungs presenting moderate bronchitis; other organs in good condition.

CASE 912.—J. M., a weak-minded man, was aged about 48 when admitted to the Middletown State Hospital, June 20, 1906; death occurred at about 58, Feb. 5, 1916. The duration of the psychosis and chorea is unknown. This patient is a brother of L. Du., case 892. At 20, the patient had been dragged half a mile in a runaway. He worked little and preferred to beg. He made threats against relatives and others and was arrested and jailed for annoying people. The reflexes were normal; he walked and turned round firmly; twitching (mostly of narrow range) was present everywhere, but was under control for a short time; the shoulders squirmed and the head moved. He talked readily, but with jerky pauses and fragmentary incomplete statements. He was inferior and had delusions that a brother was poisoning him, but he had some understanding of his whereabouts and of current events. He usually did nothing. While for the most part tractable, he was supercilious, domineering and irritable if crossed. Attempts at lumbar puncture were unsuccessful. The jerking gradually became a little worse. In 1912, speech was still fairly intelligible; in 1913, little could

be understood and it was difficult to get his attention. In May, 1914, he was much run down and difficult to understand; he was evidently disoriented. Death from pulmonary tuberculosis occurred Feb. 5, 1916. A diagnosis of tuberculosis had been made in the fall of 1915. An autopsy was performed but the time postmortem was not stated. It revealed emaciation; dura adherent; excess of cerebrospinal fluid (three or four times the usual amount); general shrinkage of the brain, without gross lesions; consolidation and tubercles in both lungs.

Case 922.—L. S. (age not stated), was admitted to St. Lawrence State Hospital, June 27, 1909. The great grandfather, great uncle, paternal uncle and cousins had chorea, with distant relatives choreic and epileptic; no chorea was mentioned as occurring on the mother's side. The patient had two illegitimate children, one slightly choreic, the other a chronic bed-wetter. The patient, who was about 43 at death (estimated), had had an ordinary education. She married at about 20; the first child was born five years later, the second about three years after that. The choreic movements began after the birth of the second child and she became suspicious of the fidelity of her husband. She secured a divorce.

On admission, June 7, 1909, about seven years before death, she was poorly nourished, had irregular choreic movements, with thick voice, and inability to pronounce long words clearly, to protrude the tongue well, or to balance well. She walked in a "sprawling" manner. The knee jerks were increased, but there was no clonus. She was restless, suspicious and sometimes noisy; judgment an insight were poor. Statements made by her regarding dates were only approximately correct. In August, 1916, she was weaker, had some diarrhea, slight fever, and a small irregular pulse; two days later she was somewhat brighter, but on the following day, Aug. 28, 1916, she died. An autopsy (time postmortem not given) was permitted only on the head. The brain was said to weigh 1,155 Gm (in the laboratory, 1,280); the pia was slightly cloudy; the convolutions were considered slightly atrophic. No focal lesions were apparent. Diagnosis: Psychosis with Huntington's chorea.

Case 938.—M. B. C., a woman, was admitted at the age of 89, Nov. 16, 1916, to Central Islip State Hospital, and died perhaps in March, 1917 (date not given). The paternal grandmother "shook when old"; the father's history was negative for chorea, but he died at 50; a brother, aged 70, had chorea from the age of 35. The patient's chorea began at about 63 and continued till death. None of the patient's children were choreic, but a sister had a son and daughter, both of whom had chorea. The patient had been married but became a widow early; she efficiently supported several children afterward as a dressmaker. Chorea began gradually at 63, with no mental symptoms for ten years. The chorea had progressed, when mental symptoms appeared, until she had difficulty even in dressing. One corner of the mouth appeared "drawn" about ten years before death and speech was indistinct, but no stroke had been observed. There was no special complaint of headache or dizziness. In the last seven years of life she grew much worse and even had to be spoon fed. The involuntary movements were increased by anything that interested or excited her and she saw few visitors. Memory and mind failed gradually; she became very irritable and obstinate, and lost her temper easily, at times biting and scratching. During sleep the movements ceased, but they were uncontrollable during waking hours. When questioned she was rather childish and somewhat mischievous. Speech was thick and the tongue was apparently not under control. She knew her age, but the mental state generally was hard to elicit. She had favorites among the

nurses and got along well with them, but was occasionally scolding and irritable. She had coughing spells, a rather small and irregular pulse, and she died unexpectedly.

Physically she was markedly senile; the knee jerks were active and equal, and there was no Babinski sign. The pupils apparently reacted to light. The involuntary muscular movements involved the whole body, but especially the upper extremities. They were coarse, awkward and of wide excursion. Contractions of the body muscles caused swaying or rocking with a tendency to fall She apparently was unable to pick up things. Facial grimacing and coarse rolling movements of the tongue were noted. An autopsy (date not given) was performed twelve hours post mortem. It revealed: much cloudy fluid in the pia reaching over a half inch in thickness; a small fresh, right-sided subdural hemorrhage "over the first and second parietal convolutions"; the whole brain seemed soft; old adhesions of the lungs; heart large and soft, with pale muscles, and enlarged left ventricle; coronary sclerosis; increase of connective tissue in the kidneys; gross atrophy of the cerebrum.

CASE 942.—C. V. C., a laborer, aged 54, who was found wandering confusedly about the streets of Buffalo and sent to the Erie County Home two years before, was admitted to Gowanda State Hospital on June 9, 1911. A brother wrote that the mother had suffered from chorea for fifteen years previous to death. At the Erie County Home he would disrobe and walk about in a nude state; he believed himself to be a drum major. When committed, he was overtalkative, with rambling speech, but was oriented for time though not for place. He became idle and contented, made numerous date discrepancies and lacked insight into his condition. Physically, he showed unsteady gait and loss of coordination, twitchings of the arms and of the tongue, but could for example comb his hair quite well. He became morose and increasingly idle. On March 24, 1916, he developed mumps; on March 28, pneumonia; he died April 1, 1916. An autopsy showed right lobar pneumonia, fibrinous pleurisy, healed tuberculosis of the upper lobe of the right lung, arteriosclerosis, and chronic interstitial nephritis.

CASE 944.—F. O'D., a man, aged about 54 at death, was admitted to Hudson River State Hospital, Oct. 2, 1915; he died May 24, 1917. He was "a member of a well known choreic family" of Duchess County (W. L. R. family). The patient was born in the town of Washington and always resided in that vicinity. For several years prior to admittance, he had been growing increasingly nervous and irritable. Gradually, on account of the mental and physical condition, he became unable to follow the trade of blacksmith. The onset of choreic symptoms appared about nine years before death, at about the age of 45; they gradually became more pronounced and seriously interfered with locomotion. He became careless in habits, went about improperly clad, stopped passers-by, frequently flew into a rage on little or no provocation, threw articles at his wife, and threatened her life. He was placed in jail, then adjudged insane, and sent to the hospital. Here he was at first restless, got out of bed every few minutes and demanded release.

Choreic movements involving the muscles of locomotion and speech were constant. Mental examination showed the repetition of certain phrases to be especially prominent. Answers were not always relevant, but usually intelligent. He worried because he could not afford to live in the hospital, said he should have been sent to the almshouse, accused his wife of infidelity with a son-in-law. He denied having assaulted her. There was no evidence of hallucination. He did not know the name of the place but gave the date correctly. Memory

was poor for routine events at the time of admission, but he gave dates concerning family history surprisingly well. There was lack of judgment and insight. He denied nervous or mental disorder and said that he could earn his living as well as ever.

Physical examination showed an elderly, poorly nourished man, with choreic involvement of the entire muscular system, and a typical gait and speech of Huntington's chorea. The Wassermann reaction in blood was negative. Hyaline casts were present in the urine. Lumbar puncture gave negative results.

The patient changed very little after admission. The choreic movements continued to show but there was no increase in their extent or severity; they were absent during sleep. Physical health was fair, aside from slight cystitis and chronic bronchitis. On May 10, he was confined to bed with some involvement of the right lung; the temperature ranged from 96 to 104.6 F. Death occurred on May 24, from empyema and gangrene of the lung of two weeks' duration.

COMMENT

So much then for the material. In Huntington's chorea, various recent authors have found changes similar to the ones in my cases. Kiesselbach,[17] in 1914, mentioned especially marked atrophy of the basal ganglia, together with general atrophy of the central nervous system in this disease. This author also made nerve cell counts in the lenticular nucleus, which agree essentially with the counts detailed here. She found the globus pallidus little changed; there was also little change in the number of cells in the red nucleus, corpus Luysii and substantia nigra. Hers is the only publication, so far as I know, in which, as in my cases, the loss of nerve cells has been reduced to figures, so that one can see just what it amounts to. She thinks with Kleist and others that there must be a connection between the choreic movements and the degeneration in the corpus striatum.

No attempt will be made to settle the functions in general of the corpus striatum on the observations in the cases of Huntington's chorea, but I shall try to state whether or not there is sufficient evidence to show that the motor disorders in this group of cases are directly dependent on the lesions in this organ.

The hemichoreas which at first seemed promising give little help in deciding these points. The hemichoreas would seem to offer good material for clearing up this question, but there is little agreement in the literature on the situation or the nature of the postmortem observations in these one-sided cases. Besides this, most of the interpretations of the examinations are based on incomplete (mostly gross) examinations.

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17. Kiesselbach, G.: Anatomischer Befund eines Falles von Huntingtonscher Chorea, Monatschr. f. Psychiat. u. Neurol. **35**:525, 1914.

Among those who report lesions in the corpus striatum in hemichoreas are Anton,[18] Liepmann [19] and Lewandowsky.[19]

Lesions in the optic thalamus, or in its immediate neighborhood, are reported or are assumed in hemichorea by Monakow,[12] Oppenheim,[20] von Economo [21] and Lewandowsky and Stadelmann.[22] Bonhoeffer [11] postulates a lesion in the fibers of the superior arm of the cerebellum or in the end stations of these fibers (optic thalamus).

Still other writers, for example Mapother,[23] who found a depressed fracture of the left parietal bone, and Romagna-Manoia,[24] who reports a dural cyst in the left superior parietal lobule, assume in each instance a cortical origin for the hemichorea. Thus, agreement is far from general as to the organ or set of organs in which the inception of these unilateral movements takes place and the character of the lesion that causes them. Perhaps the optic thalamus is slightly favored over the corpus striatum, but the heterogeneous material of the hemichoreas gives little help in localizing the lesion needed to produce chorea or in defining its type.

In Huntington's chorea, there are bilateral lesions in the corpus striatum and in the cerebral hemispheres sufficiently definite and sufficiently characteristic to enable one in most cases to recognize at post mortem with fair accuracy, that this symptom complex existed clinically during life, but one is still not justified in localizing the origin of the muscular disorders, on the evidence so far brought out, to any one region.

The most marked lesions in any parts of the brain in my cases are undoubtedly those in the putamen and caudate nucleus, the newest parts phylogenetically of the corpus striatum; but the diffuse lesions in the forebrain (cortex and marrow) are also well marked and are likewise in parts of relatively late phylogenetic origin. In other words, the lesions

18. Anton, G.: Ueber die Betheiligung der grossen basalen Gehirnganglien bei Bewegungsstörungen und inbesonders bei Chorea, Jahrb. f. Psychiat. **14**:141, 1896.

19. In discussion of Kleist's paper at the 18th Versammlung Mitteldeutscher Psychiater u. Neurologen, Ztschr. f. d. ges. Neurol. u. Psychiat. Ref. **6**:423, 1913.

20. Oppenheim: Lehrb. d. Nervenkrankheiten, ed. 6, Berlin, S. Karger, 1913, vol. 2, p. 901.

21. Von Economo, C.: Beitrag zur Kasuistik und Erklärung der posthemiplegischen Chorea, Wien. klin. Wchnschr. **23**:429, 1910.

22. Lewandowsky, M., and Stadelmann, E.: Chorea apoplectica, Ztschr. f. d. ges. Neurol. u. Psychiat. Orig. **12**:530, 1912.

23. Mapother, E.: Mental Symptoms in Association with Choreiform Dis. orders, J. Ment. Sc. **57**:646, 1911.

24. Romagna-Manoia, A.: Sulla sindrome emicoreica da lesione organica, Riv. di patol. nerv. e ment. **15**:585, 1910.

in both instances are found in those parts which are of late development but, without further evidence, there is no more reason to assume that the disorder in motion originates in the diseased putamen and caudate nucleus than in the other abnormal parts of the mechanism of the diseased forebrain.

It seems impossible, by merely collecting and comparing the reports in the literature on chorea with my own cases, to pick out the essential lesion in any of the choreas, Huntington's chorea included. Not only are the reports extremely variable, with the reported lesions varying in site from spinal cord to basal nuclei, cerebellum and cerebral cortex, but also in all my cases the two lesions mentioned above are constantly present in combination; on the one hand a degenerative destructive process involving the nerve cells of the putamen and caudate nucleus, on the other, an atrophic process (not to try to characterize it more accurately) affecting the nerve cells and fibers of the cerebral hemispheres, accompanied by a striking shrinkage in volume and mass of both gray and white matter of the hemispheres.

As no single unmistakable and characteristic set of lesions could be established as causal by the foregoing method, it seemed advisable to approach the problem from another side and to see whether extensive and generalized lesions in the caudate nucleus and putamen, such as those just referred to, can exist without the presence of choreic movements.

The answer to this question is fairly positive; neither in my own experience nor in the literature of this subject have I found any case presenting a diffuse and generalized destructive lesion affecting extensively the nerve cells of the putamen and caudate nucleus which did not at the same time show involuntary motor disorders of some sort: sometimes chorea, as in Huntington's chorea, sometimes double athetosis with spasms, as in C. Vogt's cases, and sometimes the tremor rigidity complex as described by Wilson. In these three groups and not in any others have I found described the extensive, destructive lesions in the corpus striatum as specified in the foregoing.

The numerous arteriosclerotic lesions of the striatum in the material at my disposal, even when bilateral, are no exceptions to these statements, for they are not diffuse and generalized destructive lesions. It is true that none of the motor complexes just mentioned (ordinary tremors excepted) were noted in any of them, but in arteriosclerosis the destruction of tissue in the striatum is in definite vascular areas and is consequently focal, with good preservation of the parts between the foci. The striatum may be riddled with lesions of this kind, but the unaffected parts between the foci retain the architecture and structure of essentially sound striatal tissue. Arteriosclerosis, therefore, does not present the

diffuse destructive lesions referred to, such as occur in Huntington's chorea when no part of the putamen and caudate nuclei is normal but when both nuclei are affected throughout, unevenly it is true but not in spots, as in arteriosclerosis.

If all other parts of the brain, except the corpus striatum, were convincingly shown to be normal in the cases described by Wilson and by C. Vogt, a strong case would be made for the dependence of the motor disorders solely on the lesions in the corpus striatum. Unfortunately, in few if any of the cases of lesions of the striatum reported by these two authors or by others has the rest of the brain, and especially the cortex, been so well examined as to convince one that the lesion of the striatum was the only essential lesion present. It is easy to report the cortex and marrow as normal, but it is difficult to prove the correctness of this report.

In Wilson's personally observed cases of "progressive lenticular degeneration," he examined only two of the brains with any thoroughness at post mortem; even in these two cases much is to be desired in the examination of parts other than the corpus striatum. The same fault may be found with C. Vogt's cases, when even the extremely shrunken and obviously abnormal globus pallidus receives scant mention, and the rest of the nervous system, except the striatum, is, practically speaking, dismissed in short order as normal.

In my cases of Huntington's chorea, all of which showed degeneration in the striatum, examination of other parts of the nervous system is admittedly defective; nevertheless, changes of marked grade are exposed by the scales and are proved by the microscope to exist in cortex and marrow, yet I am unable to state with any precision just what these changes are, though knowing that they exist.

Are the motor phenomena of chorea in my cases not part of a mechanism larger than that which lies within the limits of the caudate nucleus and putamen?

Is the function of this basal organ so satisfactorily established by finding constant diffuse lesions within it in cases which present clinically certain involuntary motor complexes as given above, as to justify the conclusion on this ground alone that the organ exerts, when sound, an inhibitory or steadying influence on the cortical activity, thus preventing such disordered movements from taking place? Are the studies of Wilson or Vogt thorough enough to justify the conclusions that all parts of the brain except the striatum are normal, and that solely as a result of degeneration in this organ the symptom complexes of a Wilson's disease or a Vogt's complex are produced, or is something besides the striatal condition needed to produce them? These questions, I think, still lack a convincing answer.

In general paralysis, the striatum is diffusely diseased along with the rest of the brain. In senile dementia, the caudate nucleus and putamen, together with other parts of the brain, are often loaded down with senile plaques, while the globus pallidus escapes. In arteriosclerosis, the striatum is often involved more extensively than any other part of the brain, and yet while ordinary tremors are often present, the so-called striatum complexes are absent in all of these disorders. If the striatum has separate and individual functions that can be expressed independently of other parts of the brain, these functions have not come out clearly in my studies of Huntington's chorea, for the pathologic processes in this disease are too generalized for safe correlation of the motor disturbances with any one part.

Is there, on the other hand, any likelihood that this one organ is singled out for exclusive attack by a toxic (Wilson) or hereditary (Huntington's chorea) influence? The fact that the striatum is diseased and that at the same time the motor functions are disordered does not justify off-hand the conclusion that these two things alone are in the relation of cause and effect unless the absence of disease elsewhere can be shown. That remains to be proved. Experiments on animals have been inconclusive and have failed to give the needed proof, perhaps because they were not rightly conducted.

As to the likelihood that the corpus striatum is separately and solely diseased in the cases reported by Wilson and Vogt, instances are rare (if not unknown) in which special part of an organ (the brain in this instance) is picked out by a diffusely acting agent and is attacked within strict anatomic boundaries to the exclusion of the rest of the organ in which it lies unless a special vascular influence can be shown. It is especially unlikely that a toxic substance or any factor generally distributed should be strictly limited in its action to one anatomic area in an organ though this area might show as a spot of special predilection.

In poisoning by illuminating gas, with its selective local action on the globus pallidus, there is a diffuse action as well as a local action throughout the central nervous system, although the local action is the one that has attracted attention; in various parts of the brain, on the other hand, scavenger cells carrying the liquefied products of degeneration may be generally found. The action of the poison is therefore not limited to the grossly visible focus of softening in the globus pallidus, although it is most intense here. For these reasons, cases of gas poisoning are not suitable for illuminating or establishing the function of the corpus striatum or its parts.

It would seem best then, for the present, to leave the question open as to whether (as some believe) the motor disorders in Huntington's chorea depend essentially or wholly on lesions in the striatum, while

the mental disorders depend on lesions in the cortex. Wilson's cases and Vogt's cases would surely tip the scales in favor of such a correlation, if one could accept as proved their conclusions that in their cases of lenticular disease the whole pallidum and its mechanism are normal. The latter conclusions seem to require further corroboration by others through careful examination. The mentality in Wilson's cases at least was not intact.

At any rate, my material justifies the assertion that in pure and well developed Huntington's chorea there are constant lesions of definite type in the corpus striatum and in the cerebral cortex and marrow, and these lesions, if found in a brain unaccompanied by clinical history, are characteristic enough to make a postmortem diagnosis of Huntington's chorea at least probable if not certain, for the peculiar combination of cortical changes and basal nuclear lesions is not, as far as I know, reproduced in any other disease.

ENCEPHALITIS PERIAXIALIS DIFFUSA (SCHILDER)

A CASE REPORT WITH CLINICAL AND ANATOMIC STUDIES *

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INTRODUCTION

In 1912, Schilder [1] described a new disease entity based on a personally observed case, and four other examples were identified in the literature. He designated the condition encephalitis periaxialis diffusa and endeavored to isolate it from the collective group of diffuse scleroses (Heubner [2]).

Schilder's patient was a girl, aged 14, who for a few months had complained of headaches, vomiting and disturbance of vision, and who had become very apathetic. When she was first seen the neurologic examination, aside from a choked disk of 3 diopters and narrow visual fields, gave practically negative results. The blood Wassermann reaction, however, was positive in the mother and the daughter, and lumbar puncture showed a slight globulin reaction. After a few weeks paresis of the left abducens and of the right arm and right leg appeared. A second lumbar puncture gave fluid with a pressure of 200 mm. and with slightly increased lymphocytes. The choked disks increased to 5 or 6 diopters. Subsequently, conjugate deviation to the left developed. Stupor became pronounced, with a masklike expression. Ultimately, there were contractures of the right arm and of both legs, with spasticity. The patient died after an illness of five months.

The pathologic process consisted in a widespread, severe degeneration of the white matter of both hemispheres and of the corpus callosum. The cortex showed only a small focus on the right side. The process stopped at the fibrae arcuatae and at the basal ganglia.

Macroscopically, the diseased tissue had a yellowish appearance and an abnormal consistency, and showed in parts a cystic degeneration. The microscopic examination showed a destruction chiefly of the myelin sheaths, the axis cylinders being spared to a certain degree. There were protoplasmic glia cells, an

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* From the Surgical Clinic and Laboratory of Dr. Harvey Cushing, the Peter Bent Brigham Hospital.

1. Schilder: Zur Kenntnis der sogenannten diffusen Sklerose (Ueber Encephalitis periaxialis diffusa), Ztschr. f. d. ges. Neurol. u. Psychiat. **10**:1, 1912.

2. Heubner: Ueber diffuse Hirnsklerose, Charité ann. **22**:298, 1897.

enormous number of scavenger cells and a slight increase of glia fibers. In some areas there were giant glia cells with regressive changes, some of the cells having multiple nuclei. The perivascular spaces were filed with scavenger cells.

Marchi staining of the spinal cord showed degeneration of the right lateral pyramidal tract and of the left anterior pyramidal tract, as well as of the posterior roots.

In his account of the case, Schilder emphasized the similarity of the process to multiple sclerosis and ascribed the disease to a toxic agent affecting the myelin sheaths. Since his report, approximately forty cases in man and one in the monkey,[3] with similar anatomic observations, have been reported by different authors as cases of "encephalitis periaxialis diffusa" or as "diffuse sclerosis" or "encephaloleucopthia scleroticans progressiva." It is, however, doubtful if all of these reported cases really deal with the disease defined by Schilder. Krabbe,[4] and Claude and Lhermitte,[5] for example, have described cases showing a striking perivascular arrangement of the foci of degeneration. Cassirer and Lewy's case [6] probably is a glioma, since glia cells had broken through into the pia. In the cases reported by Siemerling and Creutzfeldt [7] and by Urechia, Mihalescu and Elekes [8] the malady was complicated by a bronzing of the skin.

In only a few details have subsequent communications surpassed Schilder's first description of the lesion. It is known today that the axis cylinders may be damaged more severely than Schilder assumed in the beginning. It is now appreciated that certain cases strongly suggest an inflammatory process owing to the perivascular infiltrations by lymphocytes and even by plasma cells, whereas other cases are of a more degenerative type, in which the infiltrations consist mainly of scavenger cells with a few lymphocytes.

The clinical course of the disease can be briefly characterized as follows: Though the age of the onset has varied from the first years of life up to 60 years (Guttmann [9]), the malady usually occurs in the

3. Schröder: Encephalitis und Myelitis, Monatschr. f. Psychiat. u. Neurol. **43**:146, 1918.

4. Krabbe: Beitrag zur Kenntnis der Frühstadien der diffusen Hirnsklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **20**:108, 1913.

5. Claude and Lhermitte: Leucoencéphalite subaigue à foyers successifs, Encéphale **15**:89, 1920.

6. Cassirer, R., and Lewy, F. H.: Die Formen der Glioblastose und ihre Stellung zur diffusen Hirnsklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **81**:290, 1923.

7. Siemerling and Creutzfeldt: Bronzekrankheit und sklerosierende Encephalomyelitis (diffuse Sklerose), Arch. f. Psychiat. **68**:217, 1923.

8. Urechia, Mihalescu, and Elekes: L'encéphalite périaxiale diffuse, type Schilder, Encéphale **19**:617, 1924.

9. Guttmann, E.: Die diffuse Sklerose, Zentralbl. f. d. ges. Neurol. u. Psychiat. **20**:108, 1913.

first two decades. The disease begins with apathy and blindness, frequently in the form of a hemianopia. After this, neurologic symptoms, which point to foci in both hemispheres of the brain, slowly develop. Coincidentally, symptoms suggestive of tumor of the brain, such as optic neuritis, headaches and vomiting, frequently arise. Many authors report epileptiform attacks in the beginning of the disease. The picture shortly before death is usually that of a tetraplegia with spastic contractures, accompanied by blindness and loss of speech. The duration of the disease varies from a few days (Neubürger [10]), up to one or two years, the average duration being fourteen months. The disease is usually fatal; only occasionally has recovery with permanent defect been known to occur (Marie and Foix [11]).

The blood Wassermann reaction is negative, the positive reaction in Schilder's first case having been an exception. The spinal fluid is normal or shows slight increase of globulin and cells. The pathologic alteration consists in a widespread destruction of the white matter of both hemispheres, which in general spares the fibrae arcuatae and only rarely invades the cortex. The diseased tissue consists of enormous numbers of fat-loaded scavenger cells, of a few naked axis cylinders, of large neuroglia cells (astrocytes) and of perivascular infiltrations with scavenger cells, lymphocytes and occasionally also with plasma cells. Finally, there is a proliferation of the vascular connective tissue.

The cause of the disease is not known, and the many therapeutic measures which have been tried have not affected its progress. In some cases the diagnosis of a tumor of the brain was made, and an exploratory operation was done, which usually accelerated the end. The correct diagnosis has been made before death in few instances; in the second case of Collier and Greenfield,[12] in the case of Brock, Carroll and Stevenson,[13] and in the case herein reported, which was typical in its entire development.

REPORT OF CASE

Clinical History.—A schoolgirl, aged 14, was admitted to Dr. Cushing's clinic on April 6, 1926, because of abdominal pains suggesting appendicitis. The father had died from an unknown disease during the early childhood of the patient. The mother, a microcephalic who is 43 years of age, has always been somewhat peculiar, and shortly after the admission of the patient developed a depressive

10. Neubürger: Histologisches zur Frage der diffusen Hirnsklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **73**:336, 1921.

11. Marie and Foix: Sclérose intracérébrale centrolobaire et symmétrique, Rev. neurol. **27**:1, 1914.

12. Collier, J., and Greenfield, J. G.: Encephalitis Periaxialis of Schilder, Brain **47**:489, 1924.

13. Brock, S.; Carroll, P. M., and Stevenson, L.: Encephalitis Periaxialis Diffusa of Schilder, Arch. Neurol. & Psychiat. **15**:297 (March) 1926.

psychosis with catatonic features. She is still confined in a psychopathic hospital. The patient's grandmother also, at the menopause, developed a psychosis with auditory hallucinations and ideas of persecution, but without any especial emotional excitation. She is alive but is reported to be psychopathic. Two brothers of the patient are said to be healthy, but one of them, whom I met personally, gives the impression of mental inferiority. The patient had measles, chickenpox, and whooping cough as a child; pneumonia, five years before admission and rheumatic fever, two years previously, and sore throat, two weeks before admission.

Approximately a week before admission, pains developed in the abdomen, chiefly on the right side, associated with frontal headaches and vomiting.

Examination on Admission.—On April 6, the patient was very apathetic. The abdomen was somewhat tender to pressure. There was questionable muscle spasm in the right lower quadrant. A slight right-sided facial weakness was present. The fundi showed tortuous veins with haziness of the nasal disk margins, more pronounced on the right side. The tendon reflexes were active and equal. No Babinski sign, clonus or Kernig sign was present. The Widal reaction was negative. The urine was free from albumin and sugar. Examination of the blood showed 85 per cent hemoglobin and 9,600 white blood cells. Blood pressure and temperature were normal.

Course.—On April 7, after admission, the patient was quiet, sleeping most of the time but was easily aroused. She was reported to have been irrational during the night. She had been incontinent of urine. She was unable to count fingers, which may in part have been due to lack of cooperation. Examination of the fundi, however, showed more definite blurring of the disk margins of both eyes on the nasal side, more marked on the right than on the left. The slight right facial weakness was still present. There was definite weakness of the right arm but no paralysis. The biceps and triceps reflexes were normal. The finger-to-nose test was normal. There was slight impairment of sensation over the right arm. The left abdominal reflex was slightly more active than the right. The knee reflexes were equal and active; the ankle reflexes were both present, without clonus; there was a definite bilateral Babinski sign. The patient showed a tendency to repeat phrases.

April 8: Roentgenograms of the skull showed no deviation from the normal. Lumbar puncture gave clear colorless fluid under normal pressure, with two cells and no globulin.

April 12: A more detailed neurologic examination showed a well-developed girl, who lay in bed with closed eyes. She was dull and responded slowly to questions. There was slight exophthalmos. The whole head was tender to percussion; the neck was stiff and tender.

Cranial Nerves: I: There was a definite difference between the right and the left—all test odors were better appreciated on the left side than on the right.

II: There was an obvious left homonymous hemianopia to a rough test. Perimetry was impossible because of the apathy. Both disks were hyperemic; the right showed elevation of the nasal margin of 1 diopter.

III, IV and VI: The pupils were wide but equal. They reacted slowly to light, the right better than the left. There was slight exophthalmos and a fine spontaneous nystagmus.

V: Hypesthesia and hypalgesia were present over the right half of the face. There were no motor disturbances. Both corneal reflexes were absent.

VII: Paresis of the whole right facial nerve was present.

VIII: Loud ticking of a watch could be heard well on both sides. The Weber test was not lateralized. Slight spontaneous nystagmus of the eyes was

present. Station and gait could not be examined because of paralysis of the right leg (not previously observed).

IX: Taste was not examined. The pharyngeal reflexes were present.

X: There had been projectile vomiting. The pulse rate was 70.

XI and XII: The spinal accessory and hypoglossal nerves were normal.

Cerebrum: Frontal: The patient was disoriented as to the date; she believed that it was 1924 and then would correct this to 1923. When asked if it was 1926, she would say "Yes; 1927." "No." Concentration and cooperation were too poor for protracted conversation. There was a right-sided anosmia.

Temporal: At the time of examination, the patient had no aphasic symptoms, but a few days previously a tendency to perseverate had been observed. She understood all questions but responded slowly in general, saying only "Yes" and "No." She could give the names of different objects shown to her. She was able to read large print. There was a left homonymous hemianopia to rough tests.

Precentral: No convulsions occurred. There was paralysis of the right arm and right leg, with diminished muscle tone. The deep reflexes were weaker on the right than on the left side. The right abdominal reflexes were absent.

Paracentral: No astereognosis or apraxia were present.

Postcentral: Sensation to touch was diminished on the whole right side of the body.

Occipital: No hallucinations of sight were noticed.

Cerebellum: Station and gait were impossible to examine. Hypotonia of the right arm and leg and slight spontaneous nystagmus of the eyes were present. No ataxia, hypermetria or adiadokokinesia were seen.

Comment.—This examination made it clear that I was dealing with a disorder of the central nervous system of rather rapid onset which involved both cerebral hemispheres. The left homonymous hemianopia and right-sided anosmia pointed to the right hemisphere; the right-sided flaccid hemiplegia with corresponding sensory changes to the left hemisphere. A presumptive diagnosis of Schilder's form of encephalitis was made. The nature of the condition became still more distinct as the symptoms rapidly developed. Their progress from day to day as revealed in the bedside notes is as follows:

April 15: Definite motor aphasia was apparent. The patient had difficulty in finding words and showed marked perseveration.

April 16: Choking of the right disk from 1 to 2 diopters and of the left disk from ½ to 1 diopter was seen. There was a right abducens paresis. The light reaction of both pupils was sluggish, but present; the reaction to distance was absent. Slight elevation of temperature was present for the first time since admission.

April 18: There was more pronounced palsy of the right external rectus. Aphasia was extremely marked. The disks showed an elevation of 3 diopters. The left hemianopia was apparently unchanged. The patient was less drowsy than for some time. The right hemiplegia was unchanged.

April 19: Slight paresis of the left abducens was present. The left pupil was wider than the right. Choking of 3 diopters was present on the right and of 4 diopters on the left side; small hemorrhages were present above the left disk. Paresis of the right hypoglossus was present. The soft palate moved badly, especially on the right. Aphasia was increasing. Slight spasms were observed in the right arm and leg.

April 20: The white blood cells numbered 12,100 per cubic millimeter.

April 21: The patient again complained of pains in the right lower abdominal quadrant, which had been present for the past few days. Repeated examination showed questionable spasm of the rectus muscle. Rectal examination gave negative results. A second lumbar puncture gave clear fluid under somewhat high pressure. The globulin reaction was negative: there were ten cells; the total protein was 45 mg.; the colloidal gold test gave 0012200; the Wassermann reaction was negative. The blood showed 12,300 white cells.

April 23: Paresis of the hypoglossus on the right side was increasing. The soft palate moved badly and food got into the posterior nares during eating. Lumbar puncture two days previously had given some subjective relief, but no objective improvement with the exception of diminution of the drowsiness. The right hypesthesia for touch and pain was now apparently complete.

April 25: The white blood cells numbered 8,000 per cubic millimeter.

April 26: The condition of the patient was worse. She now appeared to have a vagus paralysis. Intonation and coughing seemed to be impossible. There was marked ataxia of the left arm and the left leg was now very weak. Other symptoms were unchanged.

April 27: The white blood cells numbered 9,300; polymorphonuclears, 70 per cent; lymphocytes, 26 per cent; eosinophils, 4 per cent. No achromia or polychromia was present.

April 30: The patient was unable to move the left arm and leg; she now had a quadriplegia. She yawned frequently and had marked difficulty in swallowing. She was unable to utter wishes or to move; nevertheless, she seemed to recognize the examiner and to understand his questions.

May 1: There was slight elevation of temperature. The white blood cells numbered 7,100.

May 4: The patient was found with the head turned to the right and with conjugate deviation of the eyes to the right; also slight continuous nystagmus was present. Both arms were flexed and rigid. She no longer reacted to stimuli. Breathing was difficult, chiefly confined to the abdominal and auxiliary muscles of respiration.

May 8: The previous aphonia had been replaced by periods of spasmodic screaming, suggestive of Wilson's disease, which the facial expression also suggested. There were constant chewing movements, and though the legs and right arm remained more or less rigid, the left arm showed athetoid movements. The pupils were dilated, the right more than the left; they reacted well to light. The appearance of the patient on May 8 is shown in figure 1.

May 9: The white blood cells numbered 16,400 per cubic millimeter.

May 11: Choking of the disks was still 3 diopters. All the limbs were rigid. Both arms were in flexion with continued athetoid movements of the left hand. The legs also tended to get into a position of flexion. The head and eyes continued to be turned to the right. Continuous nystagmus was present. The toes were held in the Babinski position.

May 20: The patient made constant swallowing movements but refused food; she was being fed per rectum. When moved or disturbed in the slightest, she screamed as previously described. (Professor Brouwer of Amsterdam examined the patient and concurred in the diagnosis of Schilder's encephalitis.)

May 22: The right arm was still in the flexion position with rigidity. The left arm had become flaccid; athetoid movements were more pronounced. Both legs were slightly spastic and showed the "clasp-knife" phenomenon. All quick passive movements of the legs, arms, or head caused a generalized stretching and

abduction movement of the arms and legs, which lasted for a few seconds. This reflex did not occur when the passive movements were made slowly. Thus, they were movement-reflexes, similar to the "mororeflex" of infants. The reflex could not be elicited by painful sensory stimuli. The abdominal reflexes were absent; a bilateral Babinski sign persisted. The tendon reflexes were not especially exaggerated. The head had now become turned to the left. The neck was rigid. The van den Bergh test in the blood serum was negative.

May 24: The legs were now in a flexion position with marked rigidity; there was ankle clonus on the left. For the past few days, the left arm had been moved freely with continuance of athetoid movements. The patient reflexly grasped the hand of the examiner when placed in her left palm, and the grasp did not relax. The pupils were widely dilated, without reaction to light. The head continued to be turned to the left with persistent nystagmus of the eyes. The neck was extremely stiff, and slight turning of the head to the right caused screaming. There were choreiform twitchings in the legs, especially in the left.

June 22: For the past four weeks, the patient had remained in much the same condition, with gradually failing nutrition. The right arm and both legs remained spastic in flexion; the left arm still showed spontaneous athetoid move-

Fig. 1.—Appearance of patient having encephalitis periaxialis diffusa of Schilder, May 8, 1926. The flexion of both arms, conjugate deviation of the eyes and head, and bilateral Babinski position of the great toes should be noted.

ments. Passive movements of the extremities caused screaming. There was no indication of any visual or acoustic perception.

June 26: At 5:30 a. m., without warning, the patient suddenly stopped breathing.

Summary of Clinical History.—A girl, aged 14, came into the clinic because of headaches and pain in the right lower abdominal quadrant. The patient's mother has a depressive climacteric psychosis and the grandmother has suffered for years from a paranoid psychosis. On admission the patient was apathetic. She had a right facial weakness and hyperemia of the optic disks. During the next few weeks, she developed hypotonic right-sided hemiplegia, hypesthesia for touch and pain over the whole right side, right hyposmia, and left homonymous hemianopia. Shortly afterward, a motor and later also a sensory aphasia appeared. The choking of the disks gradually increased during the next few weeks to from 4 to 5 diopters. Meanwhile the left leg became paralyzed, and all the paralyses slowly acquired a spastic character. The right arm

went into flexion contraction. The head and eyes became strongly deviated, at first to the right (fig. 1) and later to the left. Finally, the patient became entirely blind, aphasic and almost completely paralyzed, though in the left arm certain movements, athetoid in character, put in an appearance.

One lumbar puncture gave negative results; another, a slight increase of globulin and 10 cells. The blood picture was normal, with the excep-

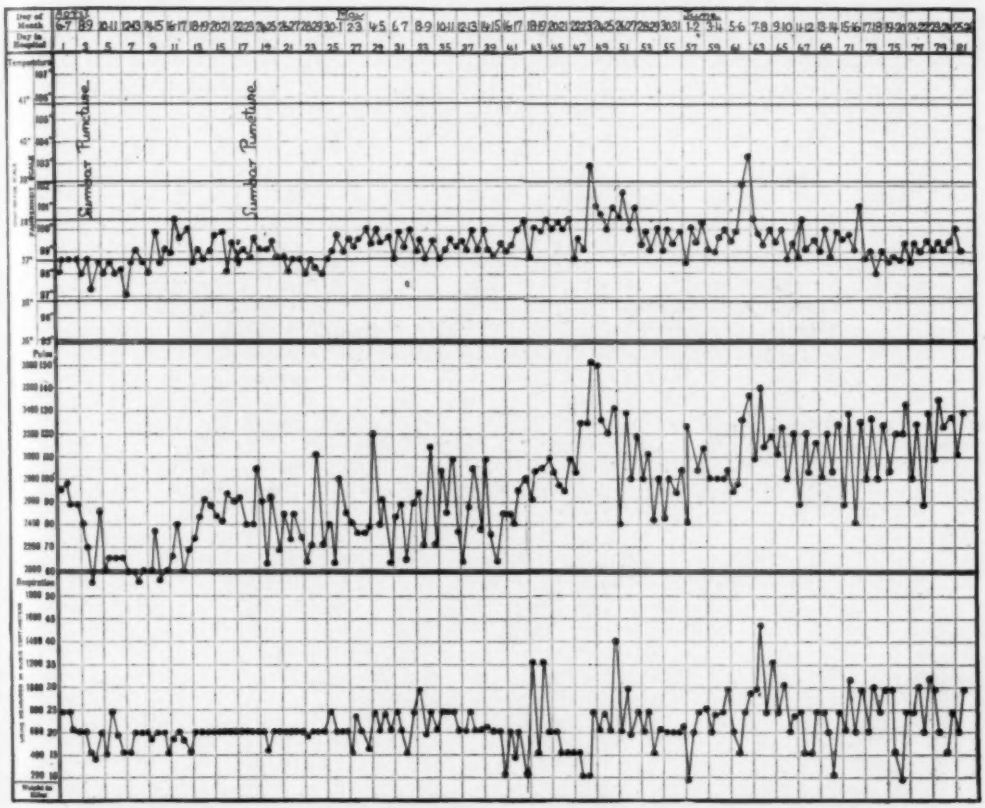

Fig. 2.—Curves showing temperature, pulse rate and respiration in a case of Schilder's encephalitis periaxialis diffusa.

tion of a slight leukocytosis. The patient grew worse in spells which were accompanied by a subfebrile temperature (fig. 2).[14] The disease lasted three months altogether.

POSTMORTEM EXAMINATION OF THE BODY

Macroscopic Examination.—Dr. Rooney examined the body five hours after death. It showed in brief poor general nutrition and a decubitus over the right

14. My thanks are due to Dr. Louise Eisenhardt for drawing this chart.

trochanter. The thymus was large. The heart and lungs appeared normal. The spleen weighed 65 Gm.; it was normal in shape and consistency. The capsule was of the usual thickness and wrinkled in a normal manner. The splenic tissue appeared purplish-red beneath it. On section, it was dark purplish-red, and the normal markings were easily made out. The pulp scraped away with little difficulty, and thin sections kept their shape fairly well. The liver weighed 930 Gm.; it was normal in shape, size and consistency. The capsule was of the usual thickness, and on section the liver tissue was normal in consistency and reddish-brown, and the markings were easily made out.

Microscopic Examination.—(Dr. Pinkerton). The heart, suprarenals, lymph glands, thymus and pituitary did not show any abnormalities. Two sections of

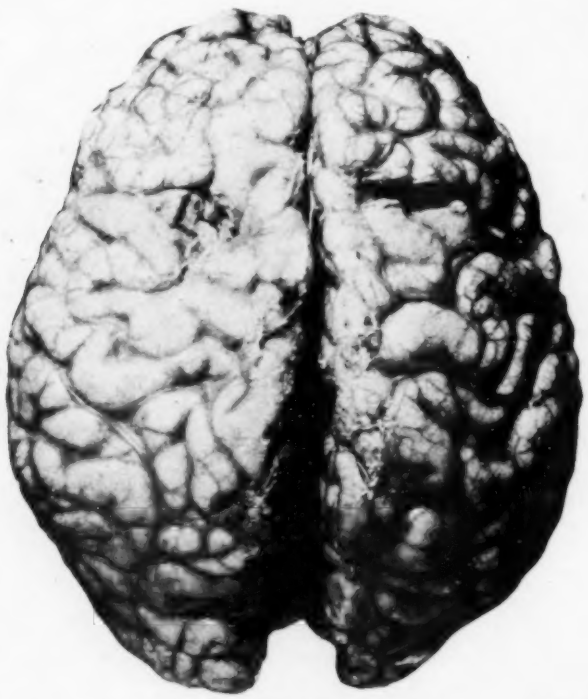

Fig. 3.—Brain from case of Schilder's encephalitis periaxialis diffusa, seen from above. The gyri of the left frontal and the right occipital lobes are shrunken.

the lungs showed a definite alveolar emphysema with the alveoli, in a few small areas, filled with red cells and serum. There was no evidence of pneumonia. The liver showed moderately diffuse congestion. A few polymorphonuclear cells in more or less focal collection were seen in the sinusoids without invading the liver cord cells. The kidneys showed marked congestion but were otherwise essentially normal.

EXAMINATION OF THE CENTRAL NERVOUS SYSTEM

After the skull was opened, a few bits of tissue from different parts of the brain were removed under sterile precautions for bacteriologic cultures. All cul-

tures were negative after incubation for seventy-two hours. The brain, which showed an excess of fluid in the subarachnoid spaces, was fixed in 10 per cent solution of liquor formaldehydi.

MACROSCOPIC EXAMINATION

The brain was small for the size of the body and showed marked convolutional atrophy, especially over the frontal lobes (figs. 3 and 4). The cerebellum with the brain stem was separated from the cerebrum by cross-section through the corpora quadrigemina. A series of frontal sections were then made in the planes shown in the diagram (fig. 5). The majority of the sections are shown in figures 6 to 12, which are in all cases viewed from behind.

The sections showed a widespread pathologic process in both cerebral hemispheres, appearing in its early stages like an inflammation and producing finally a distinct softening of the white matter. The disease involved chiefly the left

Fig. 4.—Brain from case of encephalitis periaxialis of Schilder, lateral view. Convolutional atrophy of left frontal cortex.

frontal and parietal lobes and the right temporal and occipital lobes. The fresh foci of the disease in which vessels were dilated and hyperemic were pink. The older foci were soft and grayish-white, and showed a multitude of minute holes filled with a gelatinous material, giving the tissue a sponge-like appearance. The areas in which the process was advanced were sharply demarcated from the normal tissue. When the surface of the fresh sections had been allowed to dry somewhat, this line of demarcation became elevated, the pathologic tissue being sunken in more than the normal tissue. The cortex of the convolutions which were chiefly involved was thinner and paler than normal. The morbid process stopped almost invariably at a distance of from 0.5 to 1 mm. from the cortex, leaving the arcuate fibers unchanged.

In the left (figs. 7 and 8) claustrum, there was a softening of hemorrhagic character. The left basal ganglia were severely atrophied in their whole extent. This, together with the severe destruction of the left frontal and parietal white matter, had produced dilatation of the left lateral ventricle. The involvement of the left pyramidal tract and also of the right to a lesser degree showed itself in

the secondary atrophy of the pons, which was more striking on the left than on the right side (fig. 14). In the cerebellum, there was only slight edema and hyperemia of the white matter.

In detail the coronal sections of the brain showed the following:

Section I.—This went through the tip of the frontal lobe and showed softening and beginning disintegration of approximately the whole white matter of the left lobe.

Section II (fig. 6).—This went through the tip of the frontal lobe, showed again severe degeneration of the white matter of the left hemisphere, of the corpus collosum, and of the inner parts of the white matter of the right hemisphere. There was a sharp line of demarcation between the normal and the degenerated tissue. This line lay on the dorsal parts of the frontal lobe, approximately

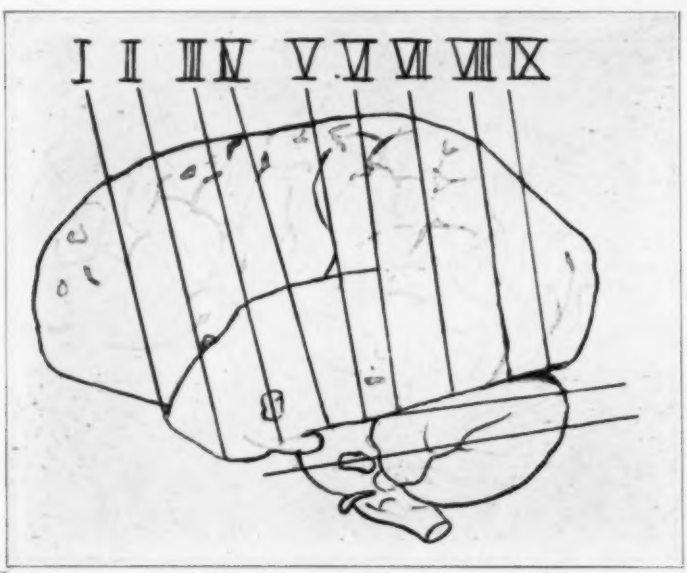

Fig. 5.—Diagram showing the distribution of coronal sections over the brain.

0.5 mm. beneath the gray matter of the cortex, always closely following its infoldings. The cortex itself was thinner and somewhat paler in the most marked zones of the disease, but showed no other change. Most of the white matter of the right hemisphere was reddish and hyperemic, showing a less advanced process.

Section III (fig. 7).—This passed through the chiasm and crossed the anterior horns of the lateral ventricle. The distribution of the degeneration of the white matter was much the same. There was a focus of hemorrhagic softening of the left claustrum. The left internal capsule had shrunken. The striae of the left caudatum and putamen could not be seen, although they were retained on the right side. The left ventricle was larger than the right, and the left striatum smaller than the right.

Section IV (fig. 8).—This passed through the corpora mammillaria. The softening in the frontoparietal white matter of the left side was advanced. It extended to and involved the corpus callosum and spread into the adjacent white

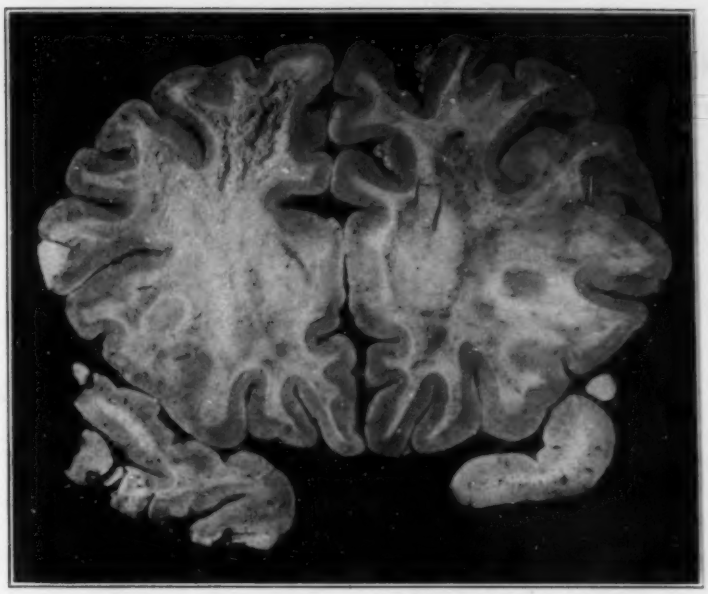

Fig. 6.—Coronal section no. 2, natural size, showing severe degeneration of left first and second frontal convolutions and hyperemia of white matter of right hemisphere.

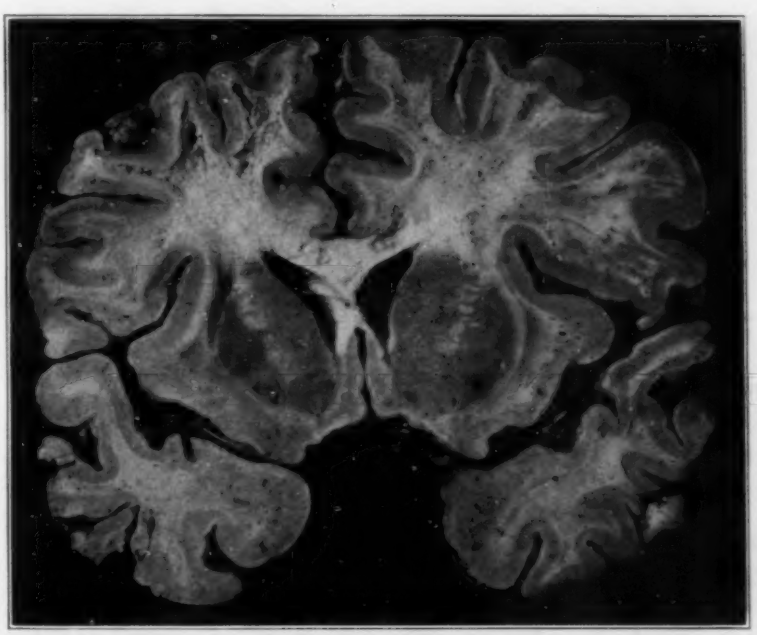

Fig. 7.—Coronal section no. 3, showing changes as in section no. 2, also shrunken left neostriatum and hyperemic area in left external capsule.

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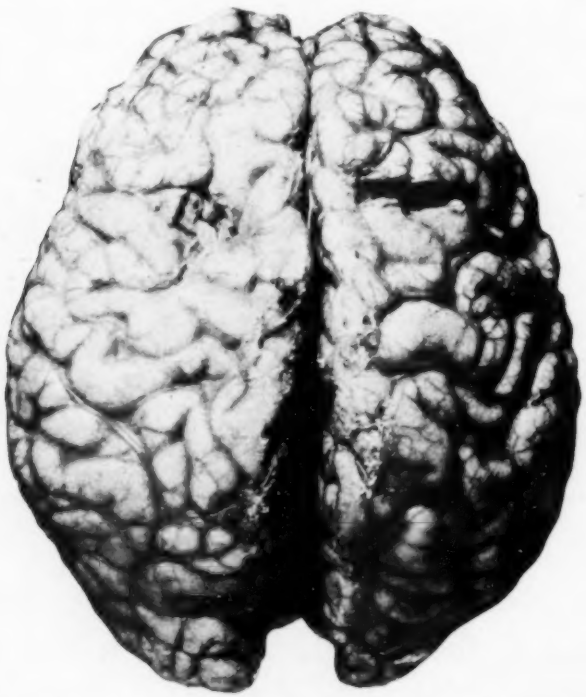

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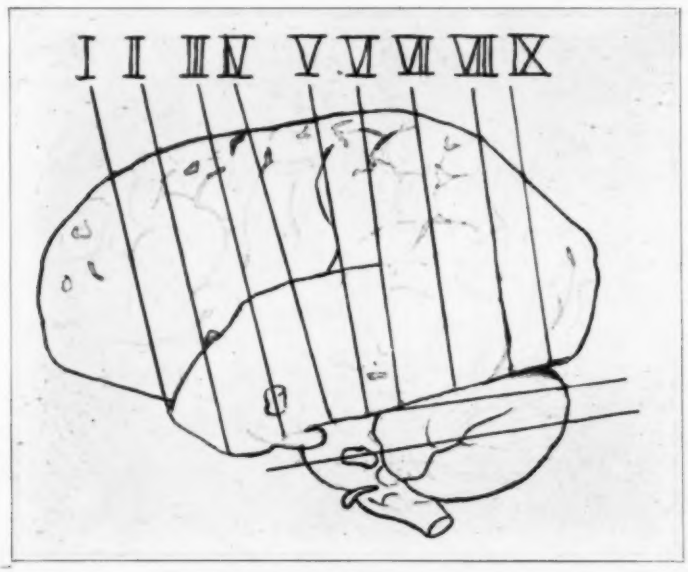

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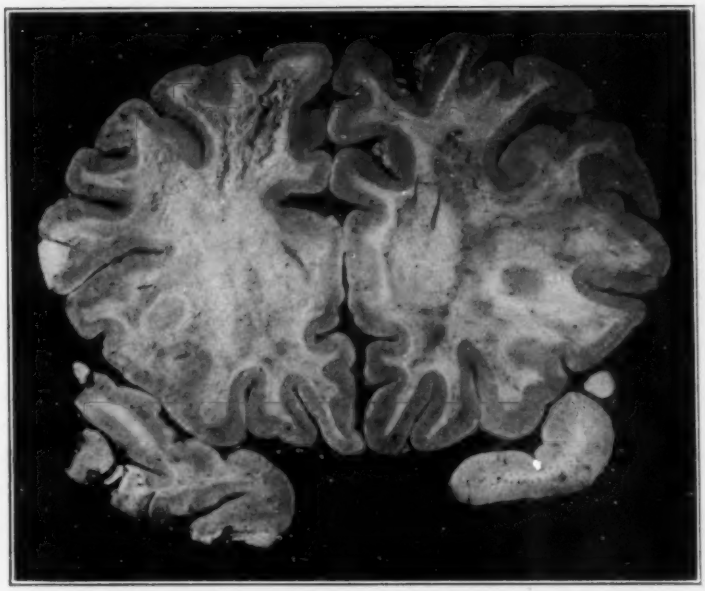

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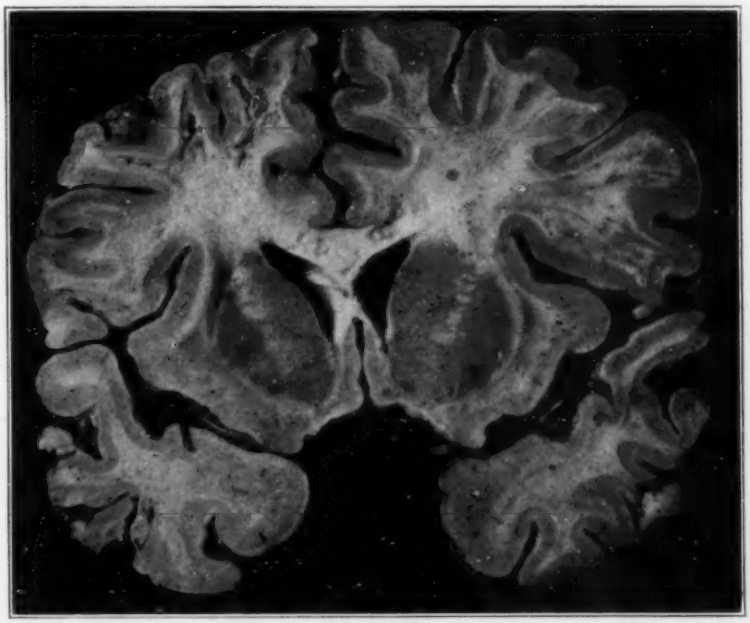

Fig. 7.—Coronal section no. 3, showing changes as in section no. 2, also shrunken left neostriatum and hyperemic area in left external capsule.

matter of the right hemisphere. The striae of the left putamen were here distinct. The left striatum and pallidum were smaller than the right, and the internal capsule was much shrunken. The left ventricle was dilated. The white matter in the right temporal lobe was softened and degenerated. In the parietal lobe of the right side, the white matter was reddish and hyperemic.

Section V (fig. 9).—This passed through the aqueduct of Sylvius. Approximately, the whole white matter of the left parietal lobe and of the right temporal lobe was here seen to be destroyed. On both sides, the softening extended into the capsulae externae.

Section VI (fig. 10).—This crossed behind the pineal body. The chief disintegration of white matter here extended into the right occiptal lobe. There was a

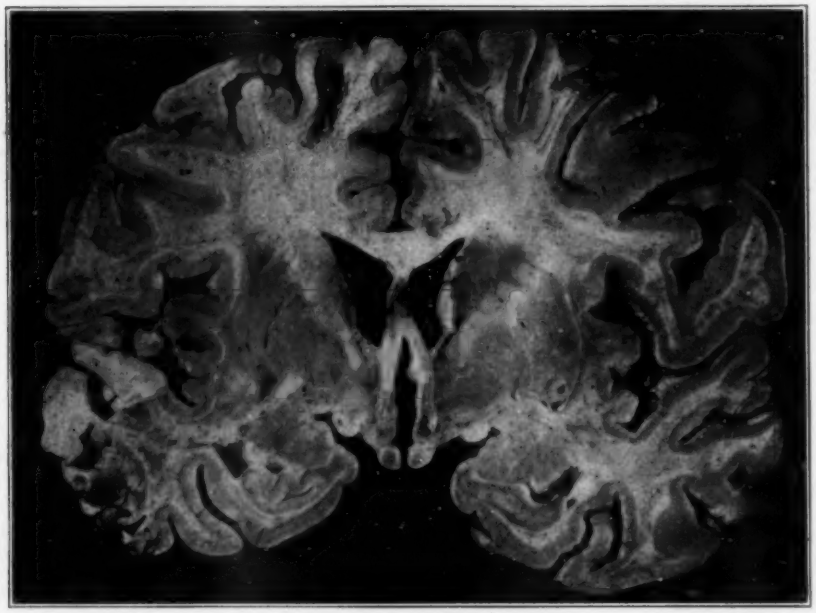

Fig. 8.—Coronal section no. 4, slightly reduced, showing severe atrophy of left caudate nucleus and of left paleostriatum.

field of fresh reddish inflammatory reaction in the right parietal lobe; there was also another fresh field in the left occipital lobe.

Sections VII and VIII (figs. 11 and 12).—These sections showed, in the left hemisphere, that the softening and disintegration of the white matter was more marked above and that the fresh hyperemic process was more marked in the lower area. On the right side the condition was just reversed, the fresh hyperemic region being above and the disintegrated areas being below.

The horizontal sections through the cerebellum and pons (figs. 13 and 14) showed that these structures were slightly edematous. There was no softening, but posterior to both dentate nuclei an area of hyperemia was apparent. The pons was asymmetrical and markedly atrophied, the left half being more atrophic than the right, due to the degeneration of the pyramidal tracts.

Fig. 9.—Coronal section no. 5, showing atrophy of left thalamus, with dilatation of corresponding ventricle.

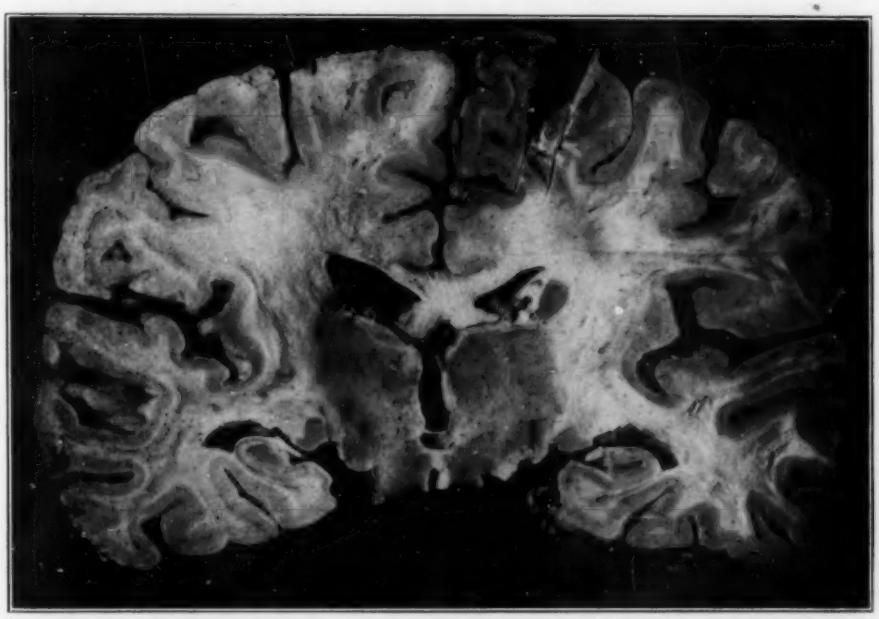

Fig. 10.—Coronal section no. 6, showing severe disintegration, particularly of the right temporal white matter.

Fig. 11.—Coronal section no. 7, showing early hyperemic lesion of right paracentral lobule; more advanced lesion of inferior parietal and temporal region. The line of demarcation between the degeneration and fairly normal white matter is clearly seen (indicated by arrow).

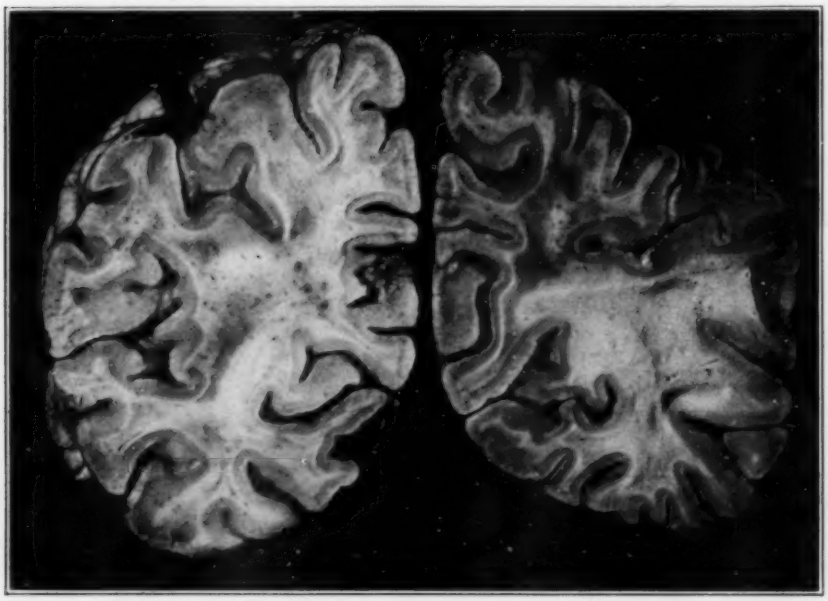

Fig. 12.—Coronal section no. 8, showing beginning and severe degeneration of both occipital lobes. The fibrae arcuatae have been spared.

Fig. 13.—Horizontal section through upper pons and cerebellum, showing region of left dentate nucleus hyperemic.

Fig. 14.—Cross-section through lower pons and cerebellum, showing atrophy of the left half of the pons.

MICROSCOPIC EXAMINATION

Histologic Methods.—Pieces of different parts of the brain and spinal cord were put into Müller's fluid, for Weigert-Pal and van Gieson's stains, and into formaldehyde for Bielschowsky-Plein, Perdrau, hematoxylin-eosin, Loyez' myelin stain, and mucicarmine of Meyer. Other sections were stained, after fixation in Zenker's fluid, in phosphotungstic acid-hematoxylin and, after fixation with formaldehyde-bromide, in gold sublimate with Hortega's IVth variant and the Gans' modification of Hortega's microglia method. Pieces of the fresh formaldehyde material were stained according to Bielschowsky and Herxheimer. Finally, some

Fig. 15.—Left precentral and postcentral convolutions. Loyez; × 5. The disintegration spares the fibrae arcuatae.

combined methods were used (gold sublimate-Herxheimer and gold sublimate-thionin), which gave satisfactory pictures.

The changes shown by the usual methods for myelin may be briefly dismissed as offering nothing novel. The Loyez method, which was chiefly employed, showed that in the regions in which the severe destruction was recognized in gross the myelin had entirely disappeared (figs. 15 and 16). In general, it respected the gray matter but occasionally it might have invaded it. For example, in figure 16 the left paleostriatum is seen to be affected.

In some places, the disappearance of the myelin appeared to be restricted to certain fiber tracts due, apparently, to secondary degeneration. In the midbrain,

for example, it was confined to the center of the pyramidal tract (fig. 17), and in the optic tracts it had a striated appearance (fig. 18). The spinal cord (fig. 19) showed a certain pallor and shrinkage of the pyramidal tracts, especially on the left, but the demyelinization was not extreme.

In describing the histologic changes more in detail, I may begin with the slightest changes, which macroscopically showed themselves as a reddish coloration of the tissue with hyperemia of the blood vessels. From the early stage, one may

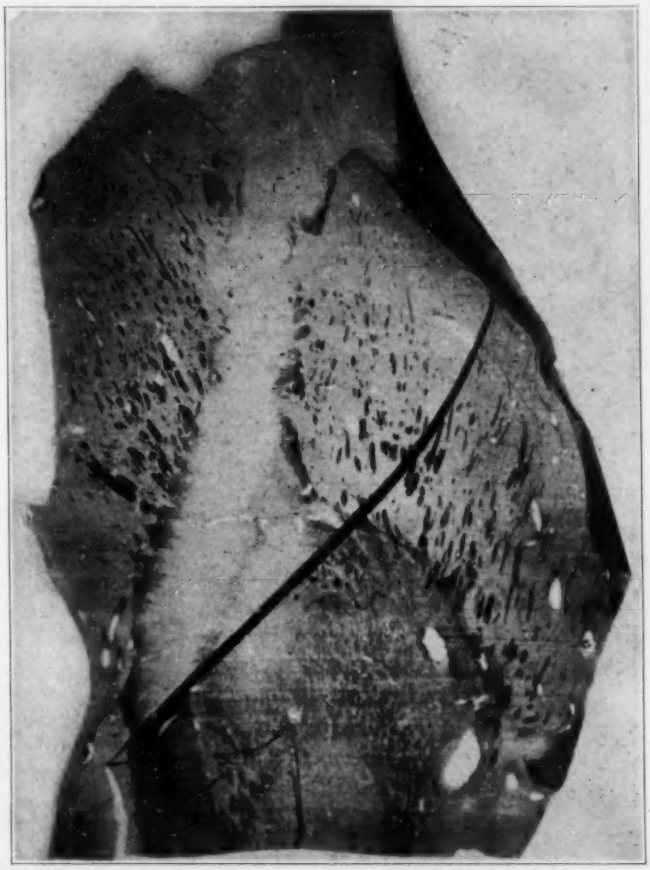

Fig. 16.—Left neostriatum and paleostriatum. Loyez' stain for myelin sheaths, showing extensive degeneration of internal capsule, extending into paleostriatum. Enlarged × 5.

progress to the more severe degenerations, and he may observe how the tissue finally changes over into the sponge-like, grayish-white substance which is filled with a gelatinous fluid.

The most striking appearances of the beginning degeneration, looked at under low power, was the large number of round or mulberry-shaped holes which were everywhere equally distributed (fig. 20). Further study showed that these holes contained a substance which could be stained with special methods. It stained

metachromatically red with thionin and toluidin, acquired a faint blue stain with hematoxylin, and became intensely red with Meyer's mucicarmine. These color reactions are characteristic for certain chemically undifferentiated substances which are grouped under the term mucin. This variety of mucinoid degeneration of the brain has been described by Grynfeltt in senile brains.[15] It has been found by Pélissier[16] in a case of hepatolenticular degeneration and has been seen by Lhermitte, Kraus and Bertillon in encephalitis.[17]

Fig. 17.—Cross-section through midbrain. The right peduncle is cut off. The left shows a large area of degeneration. (The sides in the picture are reversed.) Fine holes of mucoid degeneration appear in the capsule of both red nuclei. Loyez; × 5.

15. Quoted by Pélissier: Mucocytes et leur signification dans le processus d'inflammation chronique des centres cérébrospinaux, Communication a la Soc. de Biol., Dec. 22, 1923.

16. Pélissier, G.: Syndrome Wilsonien consécutif à la névraxite epidémique, Thèse de Montpellier, 1924.

17. Lhermitte, J. J.; Kraus, W. M., and Bertillon, F.: Mucin-Like Bodies in the Central Nervous System in Epidemic Encephalitis, Arch. Neurol. & Psychiat. **12**:620 (Dec.) 1924.

The development of these "plaques muqueuses" could be seen in some of the sections, especially in those taken from the left occipital lobe. In many of the round glia cells in the white matter, the protoplasm began to swell to enormous dimensions, and the cells stained red with mucicarmine (figs. 21 and 22). Finally,

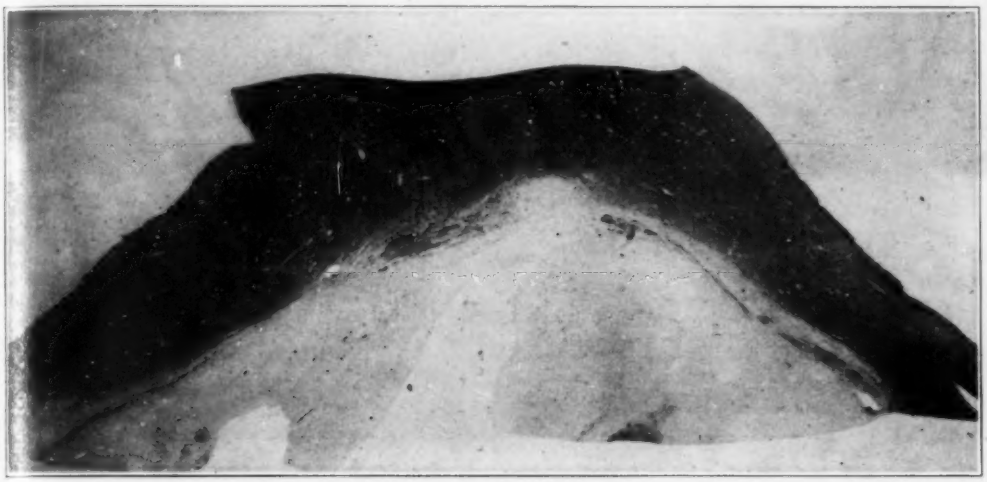

Fig. 18.—Chiasm and optic tracts. Loyez; × 6¼. Showing two patches, which look like foci of disseminated sclerosis, and two striated foci, which look like secondary degeneration.

Fig. 19.—Cervical segment of spinal cord. Loyez; × 5. Showing shrinkage and demyelinization of pyramidal areas. Right and left reversed.

the cell membranes disappeared, and the mucicarmine-stained masses entered the surrounding tissue diffusely. When adjacent groups of these cells degenerated and became fused, the mulberry or grape-shaped form of the patches was seen (fig. 23). Afterward, the glia nuclei disappeared. The process seemed to develop rapidly, because in most parts of the brain one found only mucoid patches

without nuclei. The process, in other words, occurred exactly in the way that has been described by Grynfeltt and Pélissier.

It could also be seen that mucous masses might flow into the spaces of His around the vessels whenever mucocytes were lying near a vessel. In contrast to Pélissier's description, the patches in this case were independent of the vessels.

Fig. 20.—Frontal cortex, showing transition from beginning (right) to severe (left) degeneration. The round holes in the earlier lesion are due to mucous degeneration. Hematoxylin-eosin; × 80.

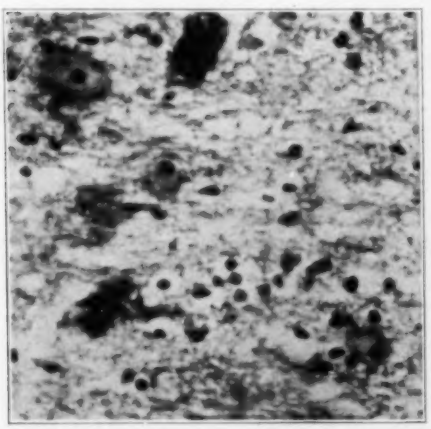

Figure 21

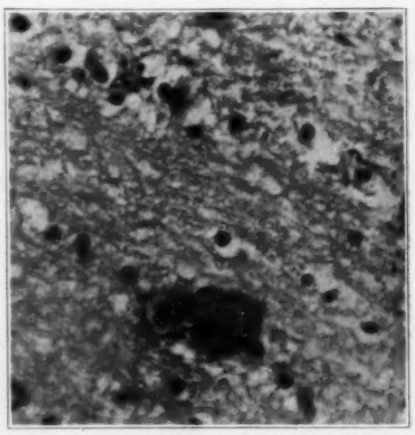

Figure 22

Fig. 21.—Mucocytes in the white matter of left occipital lobe. Hemalum, methyl-yellow, mucicarmine; × 300.

Fig. 22.—Mucocytes in the white matter of left occipital lobe. Hemalum, methyl-yellow, mucicarmine; × 300.

Comparison of those sections which showed typical mucocytes with other sections from the same block stained with phosphotungstic acid-hematoxylin (fig. 24) or impregnation with silver showed that neither macroglia nor microglia took part in this mucinoid degeneration. The degenerated cells actually proved

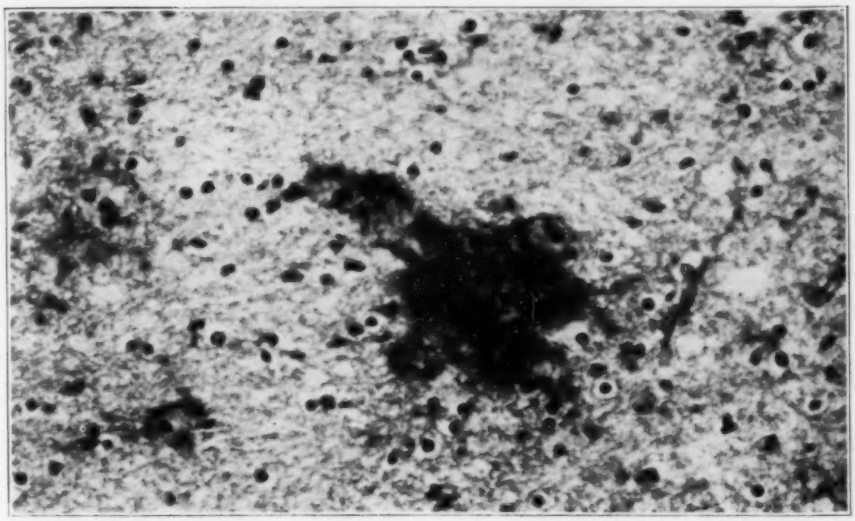

Fig. 23.—Left occipital white matter, showing mucoid degeneration. Mucicarmine, methyl-yellow and hematoxylin stain; × 300.

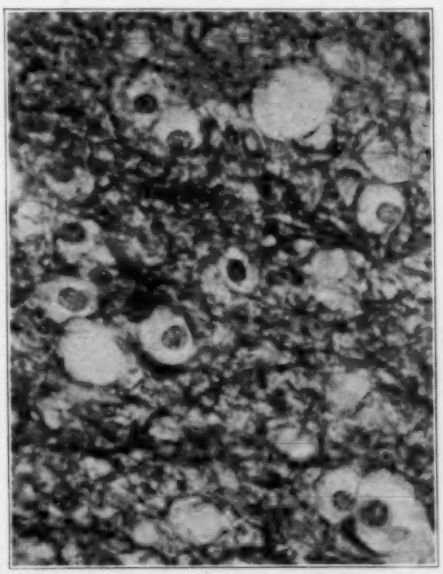

Fig. 24.—White matter of left occipital lobe, showing swollen oligodendroglia. Mallory's phosphotungstic acid stain; × 600.

to be oligodendroglia, which, with silver impregnation, corresponded exactly (figs. 25 and 26) with what Penfield and Cone have described as "acute swelling of the oligodendroglia."[18] The conclusion therefore may be drawn that Penfield's "acute swelling of the oligodendroglia" is identical with Grynfeltt's "mucocytic degeneration."[19]

The demarcation of the foci of severe degeneration appeared rather abrupt through a transition zone of 0.5 mm. thickness (figs. 15, 20, 27 and 28). This zone of transition showed a severe disintegration of myelin into drops and fragments, which changed over into substances stainable with the Herxheimer method. Mucin was still to be found in the tissue, and a few single mucocytes might appear in some areas. But throughout this zone of transition were to be seen all phases of development of the microglia cells into "rod" cells, from these to scavenger cells with prolongations and irregular outline, and finally to round scavenger cells without prolongations. There were some interesting differences in the way in which the younger and older scavenger cells became impregnated with

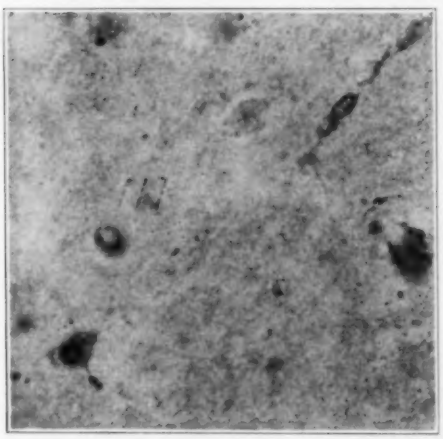

Figure 25

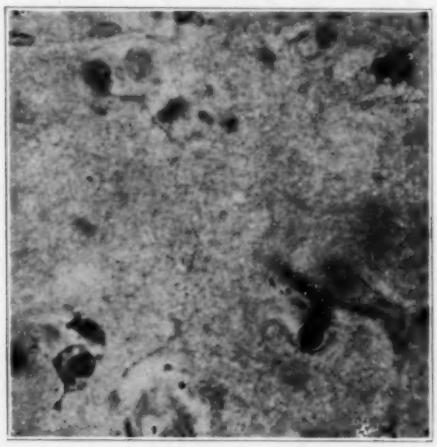

Figure 26

Fig. 25.—Cortex, showing microglia and swollen oligodendroglia. Gans' modification of Hortega's microglia stain; × 600.

Fig. 26.—Cortex, showing swollen oligodendroglia cells. Gans' modification of Hortega's microglia stain; × 600.

silver. The microglia method showed definite cell borders, especially on the younger cells (figs. 29 and 30), whereas the borders of the older ones could scarcely be seen. The Bielschowsky method showed cell borders on the older cells (figs. 31 and 32) but not on the younger ones. The Herxheimer method showed all of them to be loaded with fat (figs. 33 and 34). A few of the scavenger cells had phagocytosed mucin.

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18. Penfield, W., and Cone, W.: Acute Swelling of Oligodendroglia, a Specific Type of Neuroglia Change, Arch. Neurol. & Psychiat. **16**:131 (Aug.) 1926.

19. Bailey, P., and Schaltenbrand, G.: Die mukozytäre Degeneration der Oligodendroglia, Deutsche Ztschr. f. Nervenh. **97**:231, 1927.

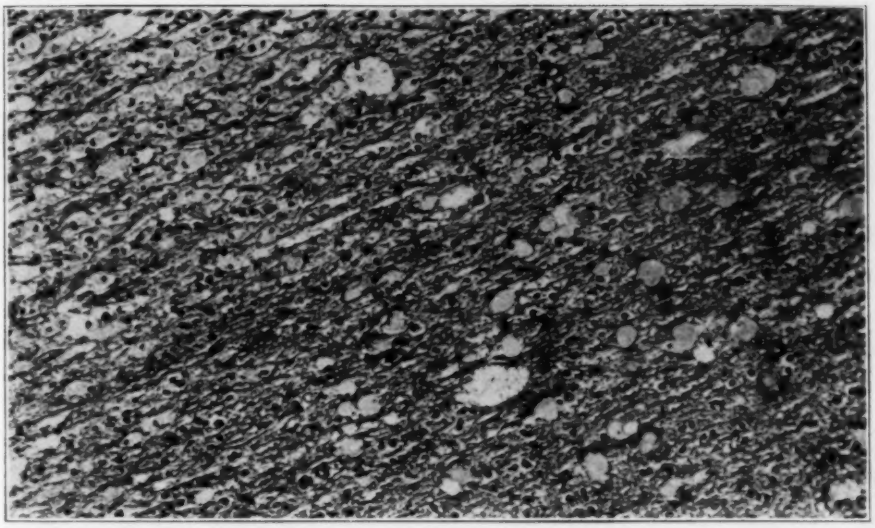

Fig. 27.—Borderline of severe degeneration below the left precentral convolution. Beginning degeneration (right), showing mucoid patches. Severe degeneration (left), showing scavenger cells. Hemalum, light green mucicarmine stain; × 150.

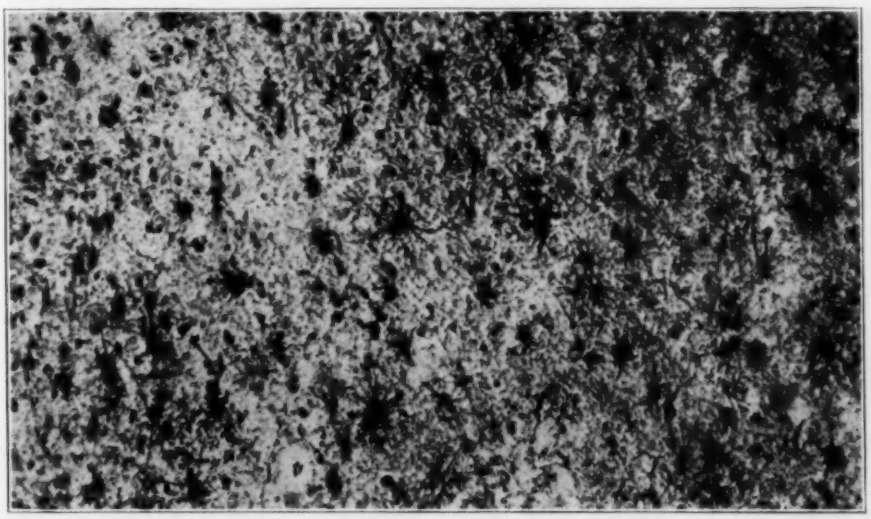

Fig. 28.—Transition from beginning (right) to severe (left) degeneration. Gold sublimate—Herxheimer; × 160. The right side shows large astrocytes; the background is dark, due to staining of myelin sheaths. On the left side, astrocytes have only short and clumsy prolongations, and myelin impregnation stops. The smaller black spots are fat droplets (stained red).

In the transition zone also, the neuroglia cells had increased in number and size (fig. 28). They might have been phagocytosed by cells that looked like oligodendroglia. The blood vessels began to show hypertrophied perivascular spaces filled with some scavenger cells and a few lymphocytes.

Mention has already been made of the round scavenger cells which abounded in the areas of severe degeneration and represented an advanced stage of the process in which the typical picture described by Schilder [1] appeared. The large astrocytes, some with two nuclei, lay at regular distances and had produced a strong network of glia fibers. The spaces of this network were filled to their limits with the fat-laden scavenger cells and a few naked axis cylinders. The myelin had entirely disappeared, and the oligodendroglia cells could no longer be found. In these regions there was an enormous infiltration of the perivascular sheaths with scavenger cells and a few lymphocytes (figs. 31 to 37). Plasma cells could not be seen anywhere. The perivascular infiltration stopped abruptly at

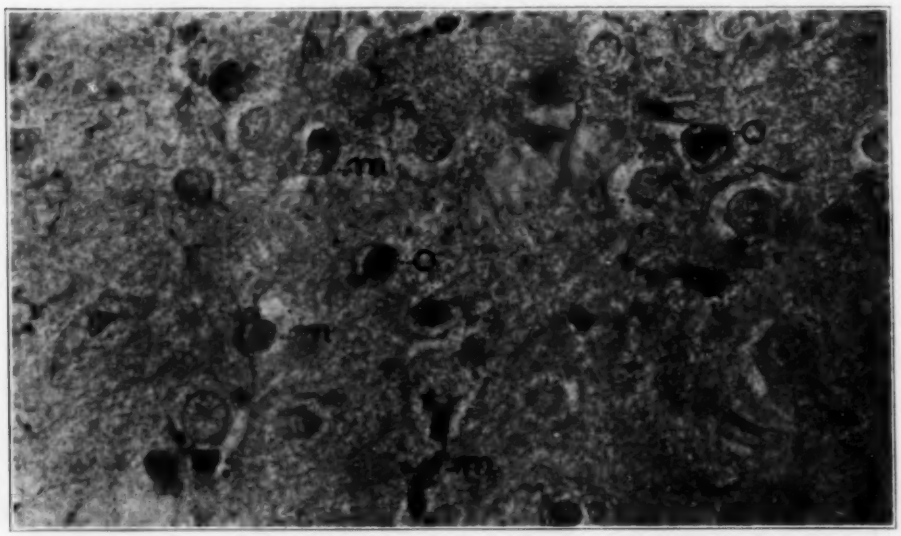

Fig. 29.—Cortex with hypertrophic microglia (*m*) and swollen oligodendroglia (*o*). Gans' modification of Hortega's microglia stain; × 600.

the line demarcating the areas of severe degeneration, from the less affected region in the cortex or just beneath the cortex.

The gold sublimate method impregnated the protoplasm of the connective-tissue cells well in the perivascular spaces and showed that they had the characteristic composition of a bundle of planes and trabeculae centered around an oblong nucleus. On cross-section, these bundle-shaped cells had a starlike appearance. The plasmatic planes and trabeculae of one cell united with those of other cells, forming in this way a system of chambers and tubes, which contained the scavenger cells. In some places, two or more tubes could be seen lying within each other (fig. 35).

In the center of the severe degeneration, some further changes occurred. The nuclei of the scavenger cells became pyknotic, and their plasma disintegrated into a granulated mass. The bodies of the big astrocytes showed definite accumulations of fat. They might lose their prolongations, and their protoplasm no

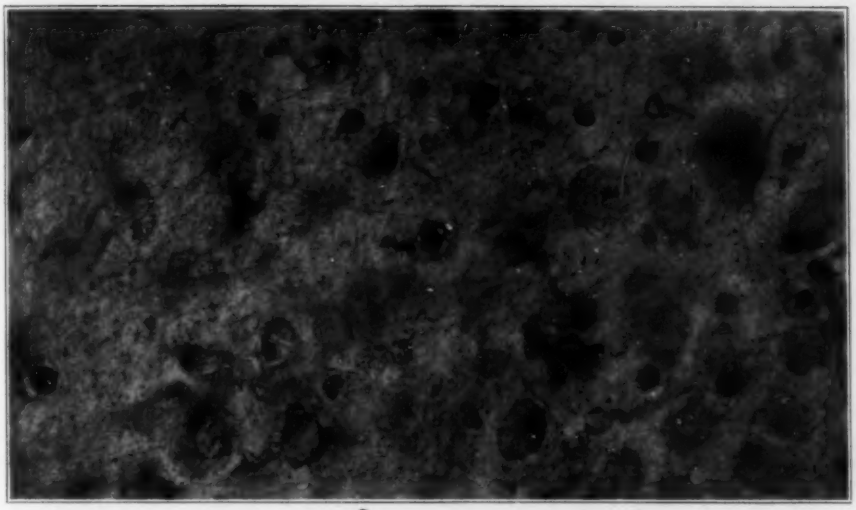

Fig. 30.—Beginning degeneration; swollen oligodendroglia and young scavenger cells with irregular silver impregnated outlines. A large astrocyte appears at *a*. Gans' modification of Hortega's microglia stain; × 600.

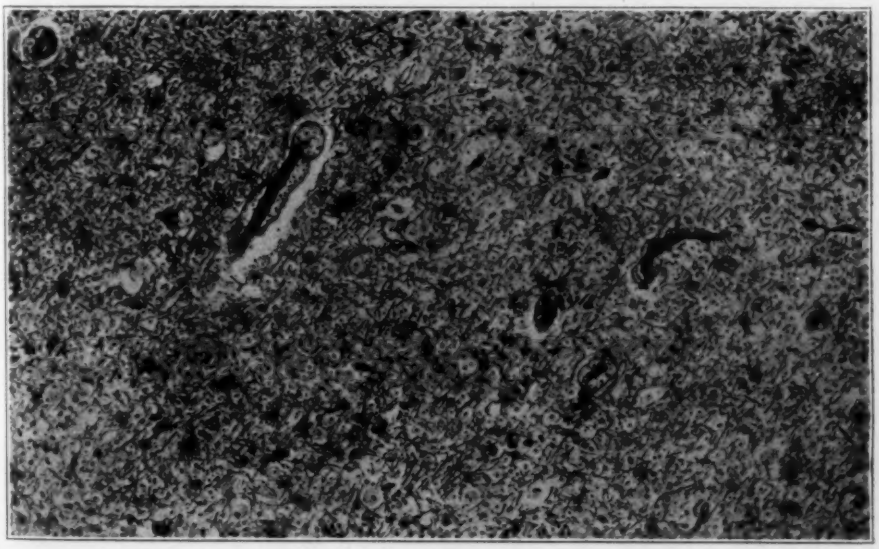

Fig. 31. Severe degeneration. Bielschowsky stain; × 80. This area, though completely demyelinated, still shows a few axis cylinders. The larger black spots are large astrocytes.

longer divided with the same speed as the nuclei, so that the picture of "gemästete" glia cells developed (fig. 38), a type of cell probably identical with what Collier and Greenfield call globoid cells. The perivascular mesodermal tissue began to invade the remainder of the nerve tissue and apparently proceeded to form a scar of connective tissue (fig. 39).

The dark-looking focus of severe degeneration around the left claustrum (figs. 7 and 8) is peculiar in that the perivascular spaces contained masses of hemosiderin indicating earlier hemorrhages.

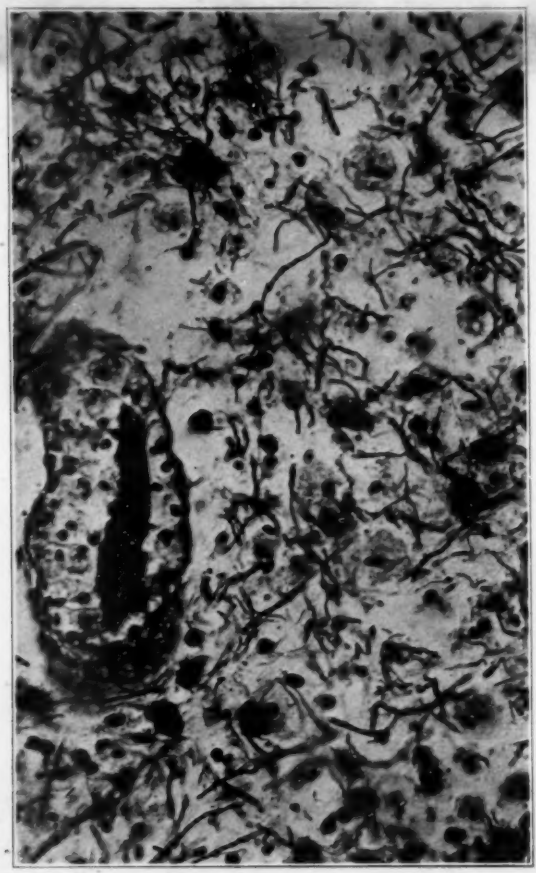

Fig. 32.—Another part of the Bielschowsky section, at a higher magnification (× 300). The pathologic tissue is composed of large astrocytes (whose prolongations cannot be seen here), scavenger cells and a few axis cylinders. The Virchow-Robin space of the blood vessel is filled with scavenger cells.

In only a few places did the severe degeneration enter into the gray substance. Such a focus could be found in a part of the left anterior central cortex, in the left paleostriatum and in the left claustrum. In the anterior central cortex, the degeneration partially reached up to the third layer. Strangely enough, the ganglion cells of the cortex were well preserved even when pathologic alterations were considerable. As a matter of fact, the changes were almost equally marked

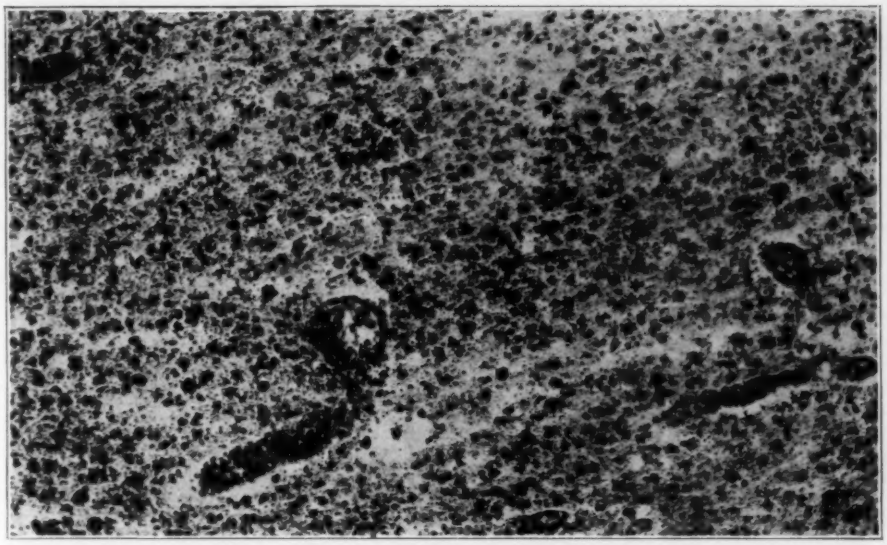

Fig. 33.—Severe degeneration of white matter. Herxheimer's fat stain; × 80.

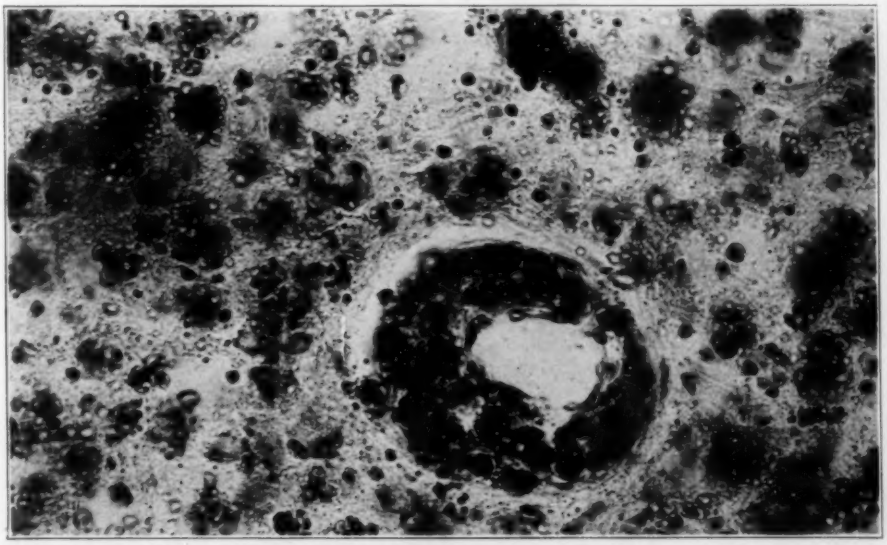

Fig. 34.—Severe degeneration of white matter, perivascular infiltration with fat-laden scavenger cells. Herxheimer's fat stain; × 300.

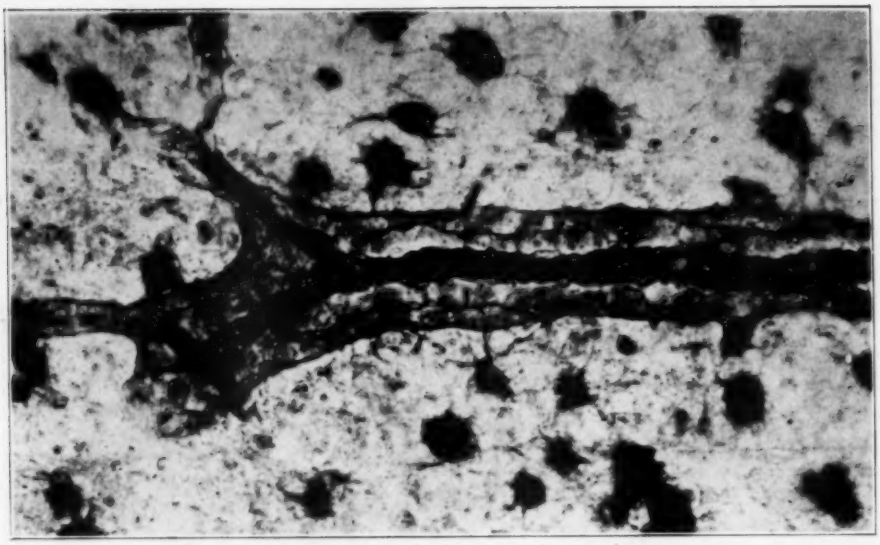

Fig. 35.—Infiltration of perivascular sheath. Gold sublimate stain; × 300.

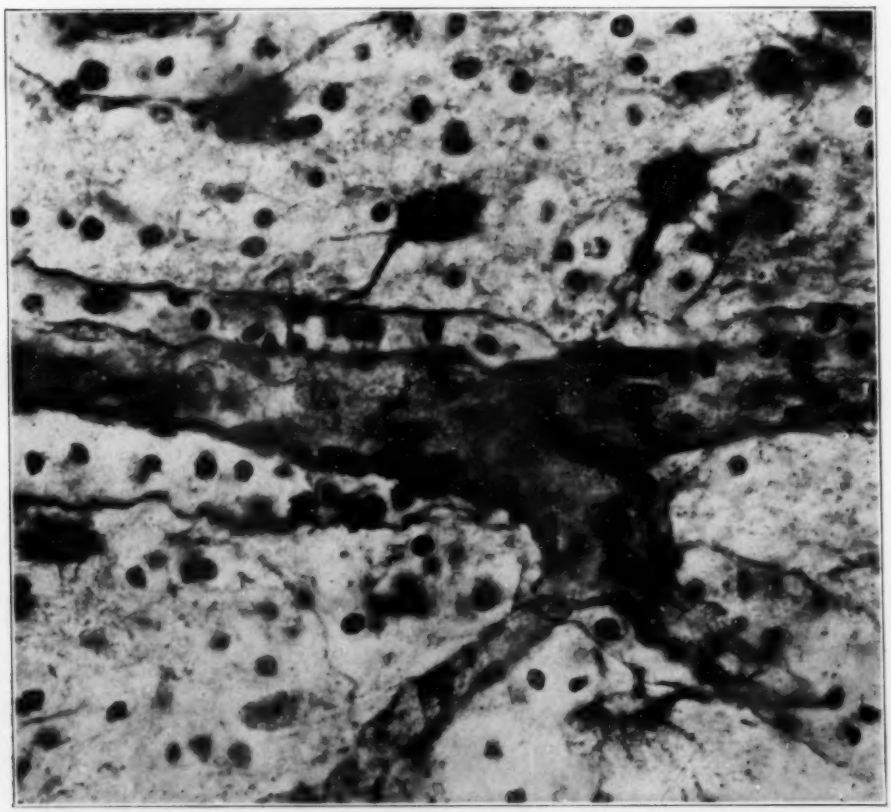

Fig. 36.—Infiltration of perivascular sheath. Gold sublimate-thionin; × 600.

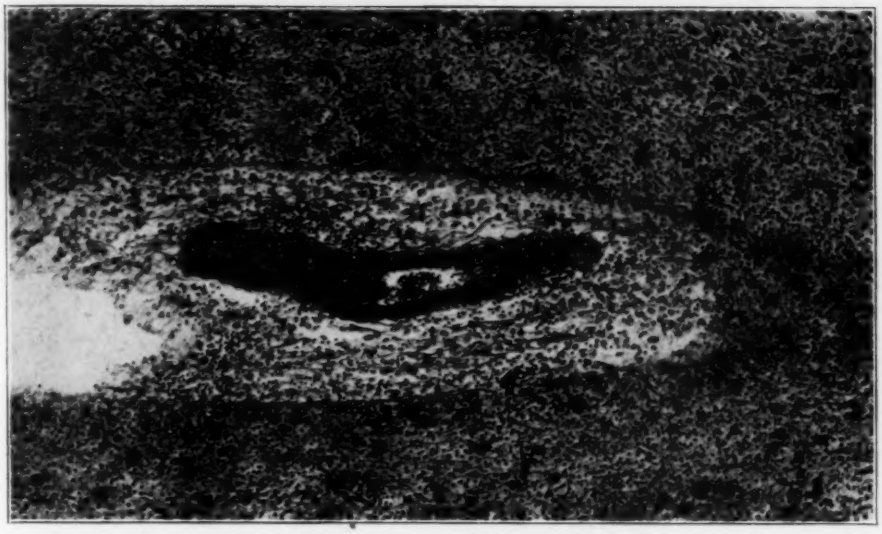

Fig. 37.—Severe disintegration with enormous perivascular infiltration around a little artery. Hortega IVth variant; × 80.

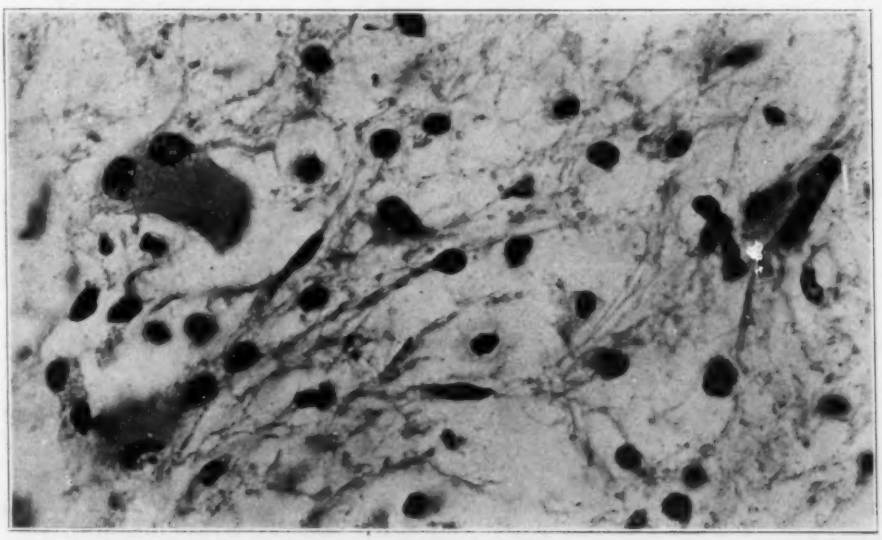

Fig. 38.—Giant glia cells (Gemästete Gliazellen) in the area of severe degeneration. Hematoxylin-eosin stain; × 600. Vacuoles from which fat has been dissolved may be seen in the cytoplasm of the multinucleated glia cell.

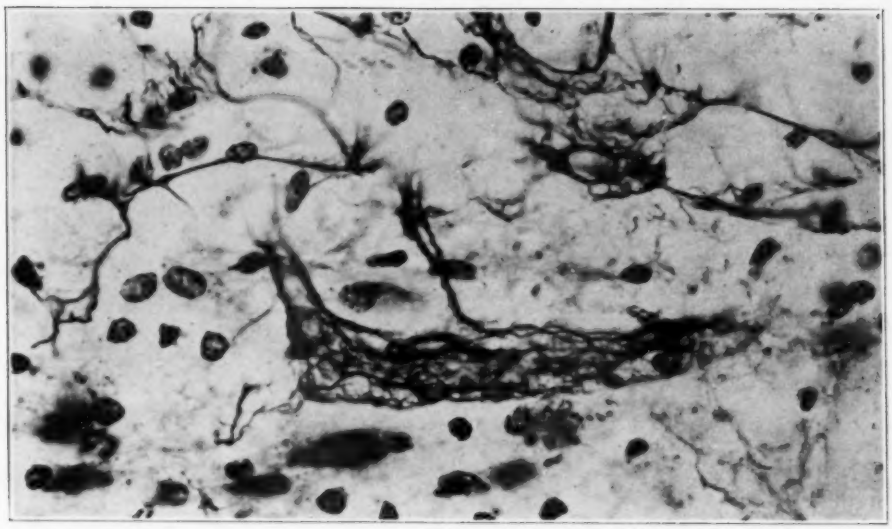

Fig. 39.—Young fibroblasts, growing out from the perivascular spaces in severely degenerated area. Perdrau; × 600. Same area as shown in figure 38.

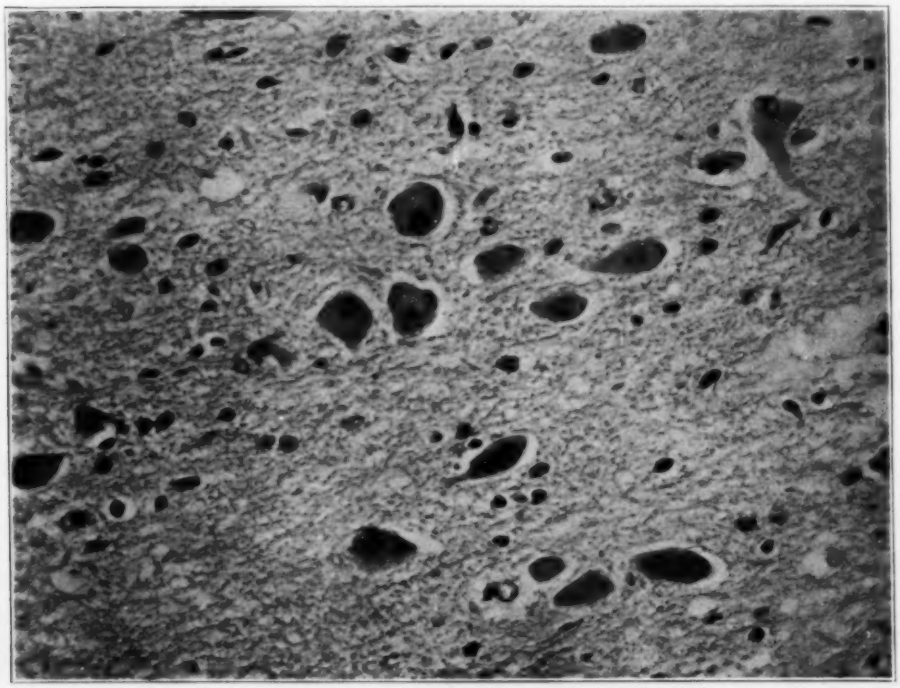

Fig. 40.—Degenerated ganglion cells of left occulomotor nucleus. Cells globoid in shape, without prolongations; nucleus eccentric. Hematoxylin-eosin; × 300.

in portions of the cortex more or less remote from the severe degeneration. The ganglion cells showed swelling and loss of prolongations. The Nissl bodies were poorly stained; sometimes there was complete tigrolysis. Many cell bodies were sclerotic. In addition to this, the oligodendroglia began to swell; the neuroglia was slightly increased, and the microglia in places had begun to change into scavenger cells. So far as could be seen, the architecture of the cortical layer was not disturbed.

The microscopic examination confirmed the macroscopic impression of the distribution of the lesions. Severe degeneration could be found, so far as examined, in the fields of Brodmann nos. 3, 4, and 44 on the left side, and in the internal capsule of the peduncle of the same side. Perhaps the focus in the left peduncle (fig. 17) was only secondary degeneration, because it was confined to the center

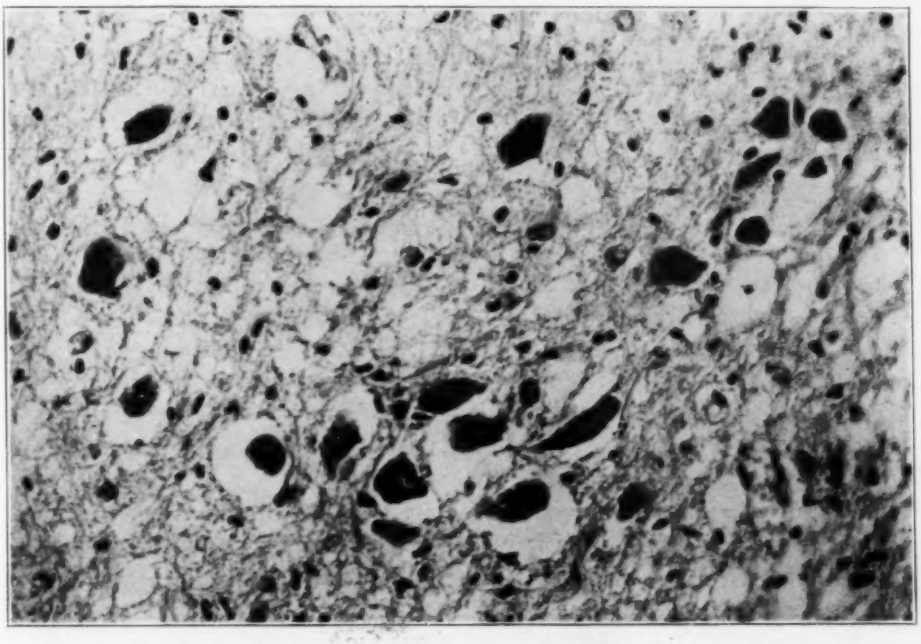

Fig. 41.—Severe degeneration of left substantia nigra. Most of the cells have lost their prolongations. The intercellular substance is sponge-like. Hematoxylin-eosin; × 300.

of the pyramidal tract. Two small patches looking like foci of disseminated sclerosis could be found in the chiasm and in the left optic tract (fig. 18). Two more foci of a striated appearance in both optic tracts might have corresponded to secondary degenerations. The white matter of the other parts of the brain, which were examined microscopically, namely, under the fields of Brodmann, nos. 1, 2, 3, 4, 10, 17, 18 of the right side, and 41, 42, 17, 18 of the left side, and also the white matter of the cerebellum showed only a beginning (mucoid) degeneration and stasis of the blood vessels.

The spinal cord, as far as examined, did not show any foci, but the areas of both anterior pyramidal tracts and of the right lateral pyramidal tract showed definite diminution and poor staining of the fibers (fig. 19). The pia arachnoid was everywhere thickened and showed a slight infiltration with scavenger cells.

COMMENT

Correlation of Clinical and Anatomic Examinations.—The distribution of the anatomic lesions explains sufficiently the severe clinical symptomatology. The most severe changes of the brain, the focus under the left central, postcentral and parietal cortex, correspond to the severe and early right-sided hemiplegia and disturbance of sensibility. The aphasia is sufficiently explained by the degeneration in the insular region on the same side. The advanced degeneration in the right occipitotemporal lobe which involved the optic radiation accounts for the left homonymous hemianopia. The later paralysis of the left leg and the final complete loss of vision can be ascribed to the widespread and more recent foci of degeneration in the right frontoparietal and left occipital lobes. It is difficult to decide how far the lesions of the chiasm contributed to the visual disturbance. Accurate perimetry was never possible. The finer striated degeneration of the optic tract may conceivably correspond to the retinal hemorrhages in the optic disks.

It is interesting that abdominal pains in the right lower quadrant were one of the first symptoms of the disease and returned later while the patient was under observation. The careful abdominal examination at necropsy did not show any local pathologic condition which could explain these pains. As the left basal ganglia proved to be surrounded by the most severe degeneration and advanced atrophy, it is conceivable that the initial abdominal pains may have been occasioned by the early involvement of the thalamus and thus may indicate the first localization of the disease.

The clinical course, the macroscopic picture and the histologic characteristics are, with the exception of the mucous degeneration which has been discovered only lately, much the same as in Schilder's first case. This is especially evident when one looks at his illustrations, and there consequently can be no doubt about the diagnosis.

The outstanding pathologic features of the disease are degeneration of the myelin with a relative preservation of the axis cylinders and pathologic changes of the glia. While the tissues in the earlier cases have been studied thoroughly with aniline stains, in my case chief attention was paid to the changes disclosed by the metal impregnations of the Spanish school, which gave certain new discoveries of interest.

Changes of the Three Glia Types and of the Connective Tissue.—The astrocytes increase in number and size, and they may become polymorphonuclear. They form a thick network of glia fibers, ultimately producing a sort of glia scar. They, however, also show signs of regressive changes, especially in the center of the severest degeneration. They accummulate fat in their protoplasm, lose their pro-

longations, and their protoplasm no longer divides with the same speed as the nucleus. So they end as the "gemästete" glia cells of the Nissl school, which are the same as Collier's and Greenfield's globoid cells. The astrocytes are phagocytosed in some places at the borderline between beginning and severe degeneration.

My studies of the microglia confirm the well-known results of del Rio Hortega,[20] who showed that these cells are migratory and phagocytic, being specially concerned with the destruction of myelin. The nucleus enlarges as well as the protoplasm, and they begin to take up droplets of foreign material. With the aniline methods, they are easily recognizable in this stage as rod cells. Later, they gradually change into the typical round "gitter" cells, lose their prolongations and are able to pass through the meso-ectodermal membrane. I shall discuss later how this important step takes place. They ultimately show degenerative changes with pyknosis of the nucleus and dissolution of the protoplasm.

The oligodendroglia cells show the earliest changes. Their ordinarily scanty protoplasm becomes visible, owing to an extraordinary swelling, and changes over into a mucin-like substance. After some time the nucleus and the cell membrane disappear and the mucin enters the surrounding tissue, where it disappears, partially by evacuation into the blood vessels and partially by phagocytosis, and in the areas of severe degeneration no trace of it remains.

According to Penfield,[21] who has made thorough studies on the pathologic changes of the oligodendroglia, this type of cell never changes over to scavenger cells. From my sections, this cannot be so positively stated, since some of them show fat-granules in the protoplasm.

In discussing the changes of the glia, one cannot ignore the connective-tissue apparatus around the blood vessels. It begins to hypertrophy as soon as the myelin is phagocytosed, and it takes over the lipoids and fat products of the scavenger cells and the scavenger cells themselves. It is worth mentioning that the infiltration of the perivascular sheaths stops immediately at the edge of the degeneration as it approaches the cortex. Thus it is improbable that the contents of the sheaths move in masses along the blood vessels into the subarachnoid spaces. In fact, the meninges show only a mild infiltration with scavenger cells. I am rather puzzled about the manner by which the scavenger cells enter the perivascular spaces. The spaces are sur-

20. Del Rio Hortega, P.: La microgliá y su transformación en células en bastoncito y cuerpos gránulo-adisopsas, Cajal's Trabaios. **18**:37, 1920.

21. Penfield, W.: Microglia and the Process of Phagocytosis in Gliomas, Am. J. Pathol. **1**:77, 1925; Oligodendroglia and Its Relations to Classical Neuroglia, Brain **47**:430, 1924.

rounded by a tightly closed membrane (figs. 35 and 36), and pictures of ameboid scavenger cells breaking through this membrane as they have been described by Held [22] could not be found. In certain places, however, two or more perivascular sheaths lie within each other (fig. 35), and this seems to indicate that the entrance into the perivascular space is less an action on the part of the scavenger cells themselves than an actual outgrowth of the perivascular connective tissue which seems to surround the scavenger cells massed in the neighborhood. The scavenger cell, according to this view, would only have to come in contact with the perivascular membrane of the vessel beyond which it cannot advance, whereupon a change of the anatomic relations takes place and the connective tissue of the Virchow-Robin space forms a new membrane around the cell. This explanation coincides with the careful anatomic studies of Jakob [23] on secondary degeneration in rabbits.

The relations between the connective tissue and the glia apparatus seem to be still more intricate. My sections show that the connective tissue always respects the nerve tissue, as long as healthy astrocytes are present. Only when the astrocytes begin to lose their prolongations does the connective tissue begin to send fibrous bands out into the former nervous tissue to form a scar of connective tissue. Figures 38 and 39 are corresponding areas in serial sections of a paraffin block. Dr. Bailey and I have found further evidence for this interrelation in some studies on the behavior of the Virchow-Robin spaces in tumors.

Interpretation of the Histologic Changes.—All of my observations indicate that each one of the glia types as well as the connective tissue has an individual pathologic reaction of its own. In part, these reactions may be considered as a "normal" reaction under pathologic conditions, as a kind of "emergency function" of the cell.

An "emergency function" of this kind would be the hypertrophy of the perivascular tissue and the outgrowth of fibroblasts into the former nerve tissue, after the degeneration of the astrocytes. The emergency function of the astrocytes themselves would be their increase in number and size and their increased production of fibers in the process of cicatrization; for the microglia, the transformation into scavenger cells and the phagocytosis of myelin. It would be interesting if a similar emergency function could be found for the oligodendroglia. Perhaps it is its tendency to form accumulations around blood vessels

22. Held: Ueber die Neuroglia marginalis der menschlichen Grosshirnrinde, Monatschr. f. Psychiat. u. Neurol. **26**:360, 1909.

23. Jakob: Ueber die feinere Histologie der sekundären Faserdegeneration in der weissen Substanz des Rückenmarke's, Nissl's u. Alzheimer's hist. u. path. Arbeiten, **5**:1, 1913.

and ganglion cells ("Gliawälle" and satellitosis) and neuronophagia, pictures that are found especially in epidemic encephalitis. A reaction of this kind is, however, absent in my case.

The mucoid degeneration of the oligodendroglia and certain changes of other glia types have nothing to do with these emergency functions. These changes may be considered as purely degenerative, like the formation of multinucleated giant cells having no prolongations, the formation of ameboid cells by the astrocytes (not present in my case), and the dissolution of the scavenger cells.

Not only do the progressive changes of microglia, neuroglia and perivascular connective tissue look like a secondary reaction, but it seems probable that most of the changes of the ganglion cells are also secondary to the severe changes in the white matter. Retrograde degeneration, poor nutrition of the cells, and general pressure may easily produce pictures of the same severity. The fact that axis cylinders may be spared by the disease process is good evidence for the secondary nature of most of the changes in the ganglion cells.

Myelin and oligodendroglia undergo an early degeneration. It is difficult to say whether a primary involvement of one of these tissues and its complete destruction may account for the rest of the changes.

Anatomic Differential Diagnosis.—Processes like the enlargement of the astrocytes, the formation of scavenger cells and the infiltration and enlargement of perivascular spaces are simply reactions to myelin destruction and are not specific for any disease picture. They can be found in multiple sclerosis, in which the axis cylinders also are preserved, though in a more complete degree. They also appear in secondary degeneration, in which the axis cylinders disintegrate primarily. The early cases of multiple sclerosis may even show perivascular infiltration with lymphocytes as in Schilder's disease. The mucous degeneration of the oligodendroglia is certainly not specific for any particular type of disease. It can be found in all cases of inflammation, intoxication, and mechanical damage of the brain. It cannot yet be decided whether or not it is always present in this disease. It was not looked for in the other cases in the literature. However, Schilder [24] found in his second case (the original case of Haberfeld and Spieler) formations which resembled "corpora amylacea." They stained faintly with hematoxylin, but metachromatically with polychrome methylene blue. The size varied somewhat. They were most frequent in the neighborhood of the focus (of severe degeneration) and in the internal capsule. The illustration (figure 8 of his paper) is similar to some of my sections, in which the mucin has undergone a stronger condensation. According to

24. Schilder: Zur Frage der Encephalitis periaxialis diffusa (sog. diffuse Sklerose), Ztschr. f. d. ges. Neurol. u. Psychiat. **15**:359, 1913.

Stanley Cobb,[25] the possibility exists that mucin indeed may change over into "corpora amylacea." Also the pictures in Schilder's third case [26] (fig. 6) suggest the presence of mucoid degeneration. Kaltenbach,[27] too, saw in his case metachromic "protagonoide Abbaukugeln" in the areas of the beginning degeneration, which probably correspond to the same process. The final softening and necrosis of the severe foci of degeneration are absent in most of the cases of Schilder's disease reported in the literature, and it seems to depend on the acuteness of the disease.

Thus, histologic pictures that may be obtained from a single slide are not sufficient to make a differential diagnosis between Schilder's encephalitis, multiple sclerosis and perhaps secondary degeneration. I do not see any difficulty in making the differential diagnosis from glioma or some rare diseases like that of Pelizaeus-Merzbacher, which is a congenital aplasia of the myelin sheaths. The final differential diagnosis between Schilder's disease, multiple sclerosis and secondary degeneration has to be made from the size and distribution of the lesions.

Etiology.—There is little evidence that the disease can be familial or inherited. There was a possible hereditary history on the maternal side in my patient. In the case of Haberfeld and Spieler,[28] the sister of the patient was said to have had the same disease. In none of the other cases reported has there been evidence of hereditary predisposition.

Most of the authors who have dealt with this disease think of an infectious agent as the most probable cause, because of the more or less frequent signs of inflammation, like the lymphocytes or even real plasma cells in the perivascular spaces. In my case plasma cells could not be found, and the lymphocytes were scanty. But the engorgement of the vessels and the occasional perivascular hemorrhages in the areas of early degeneration of my case, being similar to epidemic encephalitis, suggest an infectious origin. However, my attempts and those of other authors to find any microscopic virus by culture or by staining methods have failed. An exogenous cause in the form of an ultramicroscopic virus is therefore the most probable origin of the disease. It has, however, to be taken into consideration that this form of encephalitis

25. Cobb, Stanley: Vascular Lesions in a Case of Chronic Encephalitis Lethargica with Parkinson's Syndrome, in Soc. Proc., Arch. Neurol. & Psychiat. **16**:241 (Aug.) 1926.

26. Schilder: Die Encephalitis periaxialis diffusa, Arch. f. Psychiat. **71**:327, 1924.

27. Kaltenbach: Ueber einen eigenartigen Markprozess, Ztschr. f. d. ges. Neurol. u. Psychiat. **75**:139, 1922.

28. Haberfeld and Spieler: Zur diffusen Hirn- und Rückenmarksklerose im Kindersalter, Deutsche Ztschr. f. Nervenh. **40**:436, 1910.

is apparently a rare condition, so that some peculiar, possibly congenital predisposition may be necessary, in addition to a possible virus, to produce the severe destruction of the white matter which so unmistakably characterizes it.[29]

SUMMARY

A schoolgirl, aged 14, was admitted because of a suspicion of appendicitis. During the first examination she was apathetic and had a right-sided facial weakness and optic neuritis. During her sojourn in the hospital, she gradually developed choked disk and signs of extensive bilateral lesions of the brain, so that the probable diagnosis of encephalitis periaxialis diffusa was made. She died after an illness of three months' duration, in a state indicating practically complete disappearance of all cortical functions.

The postmortem examination of the body revealed nothing of importance pathologically. The brain, however, showed widespread softening and disintegration of the white matter of both hemispheres, the gray matter in general being spared. The process involved the corpus callosum and extended downward as far as the midbrain and the chiasm.

The outstanding feature of the less extensively involved areas of the spreading process was an abnormal filling of the blood vessels and a mucoid degeneration of the oligodendroglia (Grynfeltt), which proves to be identical with Penfield's acute swelling of the oligodendroglia. The areas of severe degeneration showed a complete destruction of the myelin, which was phagocytosed by scavenger cells of microglia origin. The axis cylinders were partially preserved. The oligodendroglia had entirely disappeared. The neuroglia had hypertrophied in number and in size of the cells and formed a thick fibrous network. The perivascular spaces were enlarged and were filled with scavenger cells and a few lymphocytes. In the regions of severest destruction there was degeneration also of the astrocytes into polynuclear forms without prolongations, dissolution of the rest of the nervous tissue, and formation of a scar of connective tissue.

This rare disease is in all likelihood caused by some ultramicroscopic virus.

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29. The bibliography given contains only a selected number of references. Complete bibliographies can be found in the articles of Bouman, L.: Encephalitis Periaxialis Diffusa, Brain **47**:453, 1924. Lewy, F. H.: Die Diffuse Sklerose, Kraus-Brugsch Hand. speziellen Path. u. Therap. innere Krankh. **10**:155, 1924. Guttman (footnote 8). Other references of interest are: Barre, Morin, Draganesco, and Reys: Encéphalite péraxiale diffuse, Rev. neurol. **33**:541, 1926. Flatau, E.: Encephaloleucopathia scleroticans progressiva, Encéphale **20**:475. 1925. Heubner (footnote 2).

THE PATHOLOGY OF AMYOTONIA CONGENITA

A DISCUSSION OF ITS RELATION TO INFANTILE PROGRESSIVE MUSCULAR ATROPHY *

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CHICAGO

Oppenheim,[1] who first described amyotonia congenita as a new clinical entity, considered the condition a primary disease either of the muscle or of the lower motor neuron. The first postmortem examination was made by Spiller,[2] in 1905, who found the central nervous system entirely normal. To date, the world's literature contains only twenty-two pathologic reports of cases diagnosed clinically as amyotonia congenita. A few authors have corroborated Spiller's first report, whereas others have reported changes within the spinal cord which have been fairly uniform.

Since amyotonia congenita has been linked by some to the myopathies and by others to the infantile type of progressive muscular atrophy, a study of the disease has some importance in a consideration of the degenerative atrophies as a group.

REPORT OF CASE

Clinical History.—A girl, aged 6 months, was admitted to the Sarah Morris Hospital on Jan. 15, 1925, with generalized muscular hypotonia. There was no familial history of similar defect; the parents had always been healthy, and the child was the first born. The presence or degree of fetal movements was not questioned. Delivery was normal; the weight at birth was 7 pounds (3175.2 Gm.), and postnatal complications were absent. The infant apparently could hear and see normally, but never sat up. At the age of 5 months the mother first noticed that the child moved its legs and arms very little, and that it gradually lost appetite and weight. It cried hardly at all and slept a great deal.

Physical Examination.—The pulse and temperature were normal. There was no adenopathy or rigidity, but a moderate degree of rachitis was noted. There was marked paresis of the lower extremities and less of the upper extremities. All of the somatic muscles were soft and flaccid. All the deep reflexes were absent. A large pad of fat was present over the dorsum of each foot. The cranial nerves were normal. Examination of the blood and urine revealed nothing abnormal.

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* From the Snydacker Fund of the Michael Reese Hospital, Nelson Morris Institute for Medical Research, and the Sarah Morris Hospital for Children.

* Read before the Chicago Neurological Society, Nov. 18, 1926.

1. Oppenheim, H.: Ueber allgemeine und lokalisierte Atonie der Muskelatur (Myatonie) im frühen Kindesalter, Monatschr. f. Psychiat. u. Neurol. **8**:232, 1900.

2. Spiller, W.: General or Localized Hypotonia of the Muscles in Childhood (Myatonia Congenita), Univ. Penn. M. Bull. **17**:342, 1905.

Necropsy.—Rigor mortis was entirely lacking. The skeletal muscles were soft and pale pink. The thymus was large, extending over the pericardium to within 3 cm. of the diaphragm and measuring 6 by 4 cm. There was slight left ventricular hypertrophy and the right ventricle was dilated. The mesenteric lymphoid follicles were hyperplastic.

Microscopic Examination.—The thymus was unchanged; there was no sclerosis, and Hassal's corpuscles were normal. The thyroid was of the fetal type, with the normal amount of colloid and epithelium. The suprarenals and bone marrow revealed no pathologic change.

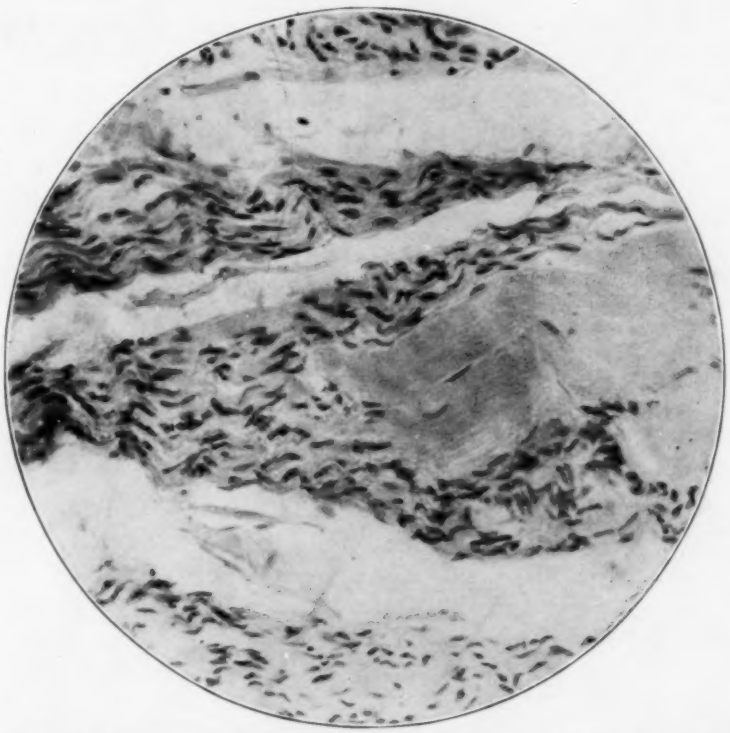

Fig. 1.—Skeletal muscle showing the small fibers which are normal except for their size. A normal fiber appears to merge into several small fibers. The sarcolemma nuclei are normal in amount for the number of small fibers in the bundle. Hematoxylin and eosin stain; × 230.

Muscle.—The diaphragm was composed of normal fibers, with only an occasional slight increase in the perimysial nuclei, and striations were preserved. The muscle of the heart consisted entirely of thin fibers, which appeared as miniatures of normal fibers in that they had normal striations and revealed no degeneration. There was, however, a slight variation in the size of the individual fibers, and the sarcolemma nuclei appeared to be abundant. The smooth muscle in the intestinal wall was normal.

The voluntary muscles (fig. 1) showed great variation in the size of the individual fibers. The largest were of normal caliber, and none was hypertrophied. The smallest fibers were again miniatures of the normal, hav-

ing longitudinal and transverse striations. Among the smallest fibers the nuclei of the sarcolemma appeared increased, but in reality they were normal for the large number of small fibers grouped together. Certain segments of the same fibers, as seen in figure 1, if followed for some distance, appeared to change abruptly from one of normal size into several small fibers. No fragmentation or degenerative changes were present. An increase of fat was not seen, and the vessels were not thickened.

Central Nervous System.—The pial vessels of the brain were engorged and a few had ruptured recently. A small amount of free blood was present in the pial meshes, some of which was already being engulfed by histiocytes. The

Fig. 2.—Anterior and posterior roots are contrasted. The poorly myelinated anterior roots are arranged in loose bundles separated by connective tissue. Weigert-Pal stain; × 24.

architectonic structure, the glia and ganglion cells were normal. In the pons and medulla, the nuclei of the cranial nerves contained cells of normal size and number.

The diameter of the spinal cord was only three-fourths that of a normal cord. In the cervical region there was a fetal lateral sulcus. The membranes were unchanged.

The fibers of the posterior root were normal throughout, but the anterior roots were small and contained few myelinized fibers (fig. 2). Between the persisting fibers there was an excess of collagenous connective tissue. No Marchi-staining degenerative products were to be found. The deficiency of

Fig. 3.—Dorsal cord; the tracts are normal. Marked myelinization of intramedullary posterior root fibers and fibers of the posterior horn has occurred as contrasted with that of the anterior roots. Spielmeyer stain; × 15.

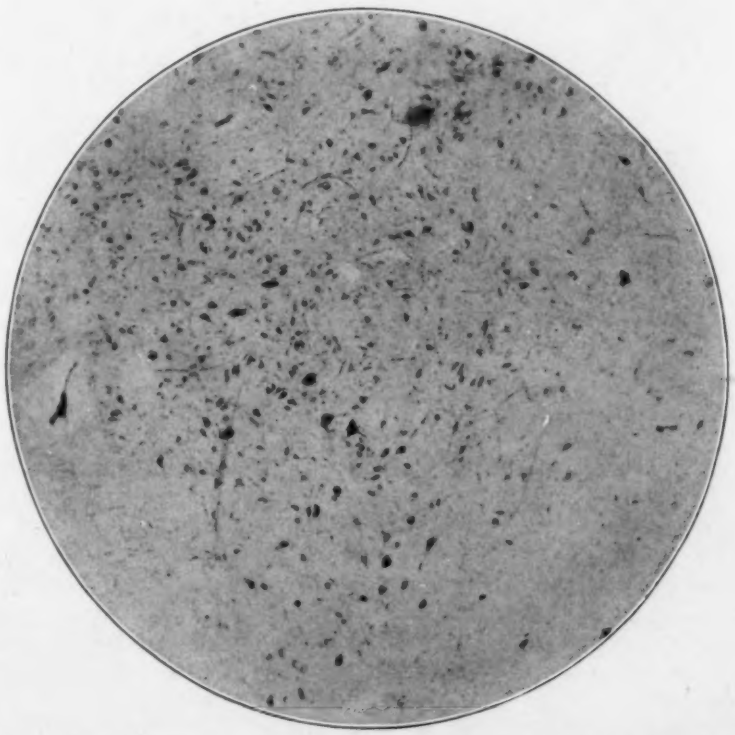

Fig. 4.—Lumbar cord; in the anterior horn only small rounded ganglion cells are present. The large cells are absent, and there is no grouping. Toluidin blue; × 50.

the myelinized fibers in the anterior roots extended to the intramedullary root fibers and to the fibers of the gray matter comprising the anterior horn. There was no abnormality in the structure of the white matter of the cord, the tracts being fully myelinized for 6 months of life (fig. 3).

An anterior horn normally contains large multipolar ganglion cells arranged in definite and usually consistent groups. No such groups of cells were seen in the cord in this case, but throughout the cord there was a marked paucity of cells of the anterior horn, contrasting sharply with the numerous and normal cells of the posterior horn, the large Clarke's column of cells and the posterolateral group of cells (fig. 4). These cells of the lateral horn were large and numerous (fig. 5).

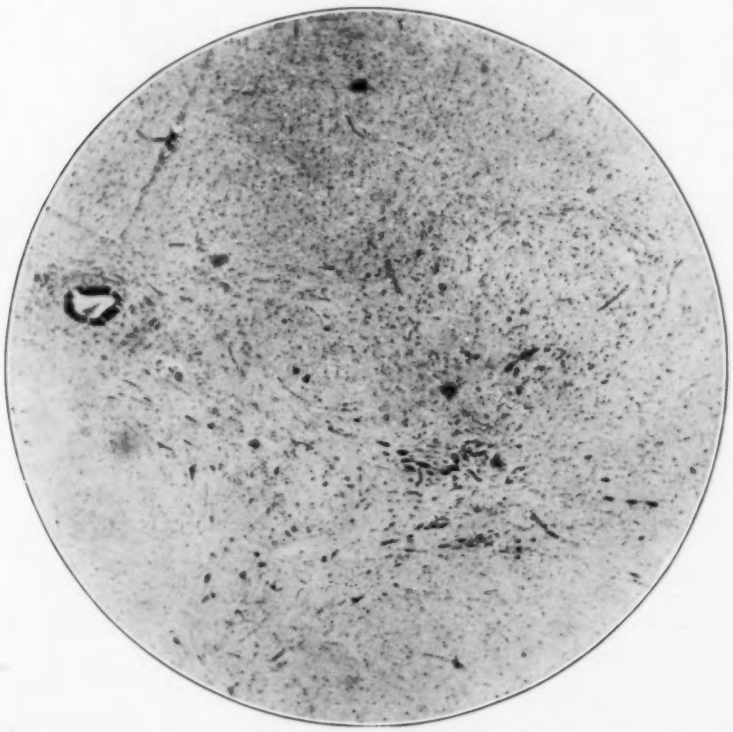

Fig. 5.—Lower cervical cord. The intermedio lateral cell group is well developed, the anterior horn cells are few and those present are small. Toluidin blue; × 40.

Occasionally a large isolated ganglion cell was noted which in the toluidin blue stain revealed coarse, blotchy Nissl bodies. By the Bielschowsky stain, the same type of cell stood out greatly enlarged, with thick processes traceable for a long distance. Within these processes was an unusually large number of neurofibrils. The sacral and lower lumbar cord contained a large number of these apparently hypertrophied cells.

Other types of cells were noted in the anterior horns. The majority were small and rounded, remarkably resembling the cells of the posterior horn and containing little chromatin (fig. 6). Other cells were long, slender and dark stain-

ing. These fusiform cells, however, were not degenerating. Nowhere were degenerative changes found in the ganglion cells. The glia cells and glia fibers and vessels were normal.

COMMENT

Clinically this case belongs in the group of amyotonia congenita as originally described by Oppenheim because of the nonfamilial history, the onset of the disease during the first few months of life, if it is not congenital, and the diffuse muscular hypotonia without localized atrophy.

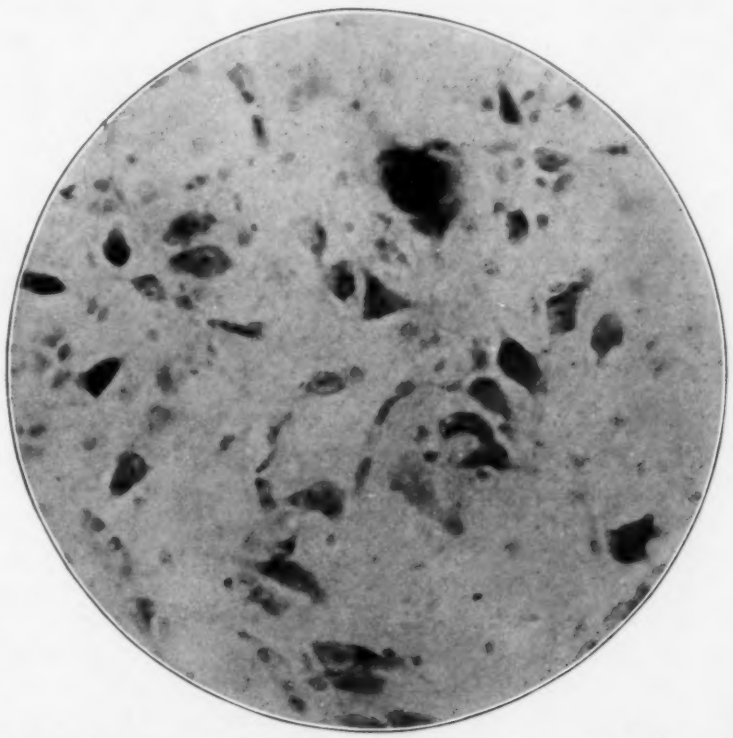

Fig. 6.—Lumbar cord, anterior horn. There is only one large cell, which is out of focus. The other cells are small, round and poor in chromatin. Toluidin blue; × 325.

It is extremely difficult to trust the parents' statement concerning the time of onset of the condition, for, as is well known, it requires an obvious defect for them to realize that their infant is abnormal. In the first few months of life there may be little difference between a normal and a hypotonic child. Collier and Holmes [3] have drawn attention to the fact that an acute infection, such as influenza or bronchitis,

3. Collier, J., and Holmes, G.: The Pathological Examination of Two Cases of Amytonia Congenita with the Clinical Description of a Fresh Case, Brain **32**:269, 1909.

seems often to precipitate the condition. Since signs of infection or toxic reaction are lacking in the central nervous system, it is possible that the acute illness first drew attention to the muscular hypotonia.

The pads of fat found on the dorsum of the feet were first noted by Collier. Pearce [4] also reported two cases in which the same fatty masses were present. Their significance is not known.

The essential pathologic changes in the central nervous system were entirely within the confines of the lower motor neuron. The absence of glial reaction, scar formation or vascular change suggests that this was not an active process, and certainly not an inflammatory or toxic condition. The simple paucity of cells of the anterior horn and the presence of cells which were either small, rounded and poor in chromatin, or long and fusiform, suggested a developmental defect. The large cells with thick processes rich in neurofibrils must be termed hypertrophic. They are of importance since they are found in other congenital defects, such as cerebellar hemiatrophy. They signify an embryonic process, as adult ganglion cells are presumably unable to hypertrophy.

The muscle changes were most marked in the skeletal muscles. There were no fatty or degenerative changes, but simply muscle fibers in miniature containing all of the markings of the normal muscle. The presence of fibers of normal size merging into many small fibers may be due to a multiple innervation of the fibers, the normal portion perhaps innervated by one of the large neurons. Hypertrophic fibers were not noted, although they have frequently been described by others.

The smooth muscle did not share in the process, and correspondingly the cell group of the lateral horn was well developed. The diaphragm was normal, as it has been in all reported cases except those of Foot [5] and Wälle and Hotz.[6] It may usually be spared because of its double nerve supply. The muscle of the heart was also of fetal type, consisting uniformly of thin fibers. The sudden death may be attributed to myocardial insufficiency, as first suggested in amyotonia by Lewis.[7] A similar explanation was given by Globus [8] for death in progressive muscular dystrophy with myocardial involvement.

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4. Pearce, N. O.: Amyotonia Congenita, Am. J. Dis. Child. **20**:393 (Nov.) 1920.

5. Foot, N. C.: Report of a Case of Amyotonia Congenita with Necropsy, Am. J. Dis. Child. **5**:359 (May) 1913.

6. Wälle and Hotz: Zur Kenntniss der Myatonia congenita (Oppenheim) Jahrb. f. Kinderh. **85**:315, 1917.

7. Lewis, N.: Heredity in Nervous and Mental Disease, New York, Paul B. Hoeber, 1923, p. 166.

8. Globus, J.: The Pathologic Findings in the Heart Muscle in Progressive Muscular Dystrophy, Arch. Neurol. & Psychiat. **9**:1 (Jan.) 1923.

REVIEW OF THE LITERATURE

For convenience a tabular form has been followed. The endocrine glands have been considered an etiologic factor in amyotonia congenita as well as in the muscular dystrophies. Table 1 shows that few cases have been reported with lesions of the endocrine glands. Smith,[9] working on Spiller's case which revealed no changes in the cord, considered the thymic deficiency primary in the development of the disease. Baudoin [10] postulated a thyroid dysfunction, while Faber [11] reports that Concetti, on therapeutic evidence (improvement after the administration of thyroid extract), believed the same.

In his case, Lewis [7] found a thyroid deficient in colloid and rich in interacinar epithelium and mesoblastic tissue. He suggested special study of the endocrine glands in future necropsies. A thyroid similar

TABLE 1.—*Endocrines in Amyotonia Congenita*

Baudoin, Spiller, Rothmann	Sclerosis of thymus and thyroid
Griffith	Suprarenals deficient in chromaffine cells
Councilman and Dun	Thymus large; thyroid small
Lewis	Increase in interacinar epithelium of thyroid

TABLE 2.—*Changes in Brain in Amyotonia Congenita*

Baudoin	Cells of the sixth and twelfth cranial nuclei have undergone chromatolysis
Collier and Holmes	Cells of the tenth and twelfth nuclei have undergone chromatolysis
Griffith	Brain large; weight, 1,542 Gm.; pia edematous
Kaumheimer	Cadaveric changes in cortical cells and vessel walls (autopsy 48 hours after death); diffuse increase in glia; tenth and twelfth nuclei affected
Rothmann	Cerebellum small; tenth and twelfth nuclei showed degeneration with increase in vascularity
Concetti	Purkinje cells abnormally shaped; all cerebellar layers small
Neumann	Eleventh nucleus contained only few cells
Spiller	Decrease in Betz cells in paracentral lobes

to that described by Lewis was found in the case here reported, and yet it was considered to be of normal fetal character. All other endocrine glands were normal except for a status thymolymphaticus, a not infrequent occurrence in infants. It is difficult to believe that a large thymus or a pathologic thyroid plays an important rôle in the changes found in the anterior horns and muscles.

Table 2 shows that in five cases the nuclei of the lower cranial nerves were affected in the same way as the cells of the anterior horn. This may mean, as Rothmann [12] suggested, that in amyotonia there is an

9. Smith, A.: Histological Changes Encountered in the Thymus and Elsewhere in a Case of Congenital Hypotonia, Univ. Penn. M. Bull. **18**:206, 1905.

10. Baudoin, A.: La myatonie congénitale (maladie d'Oppenheim), Semaine méd. **37**:240, 1907.

11. Faber, H. K.: Amyotonia Congenita, A Survey of the Known Cases with a Report of Three New Cases, Am. J. Dis. Child. **13**:305 (March) 1917.

12. Rothmann, M.: Ueber die anatomische Grundlage der Myatonia congenita, Monatschr. f. Psychiat. u. Neurol. **25**:161, 1909.

agenesis of ganglion cells with transition cases to the infantile nuclear aplasias of Moebius. Spiller's observations of a decrease in the Betz cells of the paracentral lobules have remained uncorroborated.

In commenting on the reports of degeneration of cord tracts in table 3, it must be remembered that there is a great difference between degeneration and paleness of a tract. Especially is this true in infantile cords in which myelinization may not be complete. This may account for the degeneration in some cases.

TABLE 3.—*Alterations in Cord Tracts in Amyotonia Congenita*

Marburg	All tracts deficient in myelin
Kaumheimer	Degenerating fibers in tracts
Archangelsky and Abrikosoff	Gowers' and pyramidal tracts stain poorly but no degeneration
Foot	Pallor in all but posterior columns; degenerative changes in substantia reticularis
De Villa	Slight rarefaction of pyramidal tracts
Councilman and Dun	Slight degeneration in myelin of posterior columns
Rothmann	Anterolateral tracts thinned

TABLE 4.—*Changes in Gray Matter in Amyotonia Congenita*

Marburg	Cells of the anterior horn few, small pyknotic; thickened vessels in cord; connective tissue and glial increase
Kaumheimer	Cells of the anterior horn large, swollen, vacuolated, degenerated; neuronophagia marked; Clarke's column also affected
Baudoin, de Villa, Holmes, Silverberg	Cells of the anterior horn small, reduced in number
Archangelsky and Abrikosoff	Anterior horn and Clarke's cells small and few
Griffith and Spiller	Cells of the anterior horn small and few
Foot, Wälle and Hotz	Cells of the anterior horn rounded, vacuolar degeneration and acutely swollen; glial increase; clumped Nissl bodies
Collier and Holmes	Large cells of the anterior horn reduced one third; lateral and posterior cell groups of anterior horn cells especially small
Slauch	A few cells of the anterior horn in axonal or retrograde degeneration
Lehoczky	Decrease in cells of the anterior horn, pyknosis, vacuolization; neuronophagia and degeneration in all stages
Neumann	Nissl bodies poorly stained; polygonal cells absent
Concetti, Mensi	Cells of anterior horn few, small and pyknotic
Rothmann	Cells of anterior horn few; Nissl bodies thick; increase in glia of gray matter
Mettenheimer	Atrophic changes in cells of the anterior horn
Krabbe	Few normal cells in anterior horn; cells with pale, homogeneous cytoplasm; others pyknotic; increase in glia fibers
Lereboullet and Baudoin, Spiller, Councilman and Dun	Normal cord

In table 4 it may be noted that most authors speak of a paucity of cells and the presence of small, abnormally shaped cells. However, Marburg,[13] Kaumheimer,[14] Foot, [5] Wälle and Hotz,[6] Lehoczky,[15] and Krabbe [16] report degenerative changes resembling an active process in the ganglion cells. They found swollen, vacuolated cells in various

13. Marburg, O.: Zur Klinik und Pathologie der Myatonia congenita (Oppenheim), Arb. a. d. neurol. Inst. a. d. Wien. Univ. **19**:133, 1911.

14. Kaumheimer, L.: Zur Pathologie und Klinik der Myatonia congenita (Oppenheim), Jahrb. f. Kinderh. **78**:176, 1913.

15. Lehoczky, L.: Ueber die Myatonia congenita Oppenheim und ihre Beziehungen zu der Werdnig Hoffmannschen Krankheit, Arch. f. Psychiat. u. Neurol. **71**:491, 1924.

16. Krabbe, K.: Congenital Familial Spinal Muscular Atrophies and Their Relation to Amyotonia Congenita, Brain **43**:167, 1920.

stages of neuronophagia, or an increase in glia and vascular changes. Thus the reports fall naturally into two groups: one group of cases shows few ganglion cells of abnormal shape; the other group shows actual degeneration of the ganglion cell. The significance of this fact will be considered later.

In table 5, most authors mentioning changes in the peripheral nerves use the terms degeneration or atrophy. In most reports illustrations show a decrease in the myelinized fibers separated by an increase in connective tissue. It is noteworthy, however, that cases which revealed actual degeneration of the ganglion cells showed degenerative changes in the peripheral nerves and roots. Added to these is the case of Griffith

TABLE 5.—*Anterior Roots, Nerves, and Nerve Endings in Amyotonia Congenita*

	Anterior Roots	Nerves	Nerve Endings
Marburg, Kaumheimer	Small	Increase of endoneurium	—
Baudoin	Small	Fewer fibers; Schwann cells increased	—
Collier and Holmes, Concetti	Small	Decreased myelin; fewer fibers	—
Archangelsky and Abrikosoff	Small; poor in myelin	Poor in myelin	Not found
Griffith and Spiller	Small	Degeneration; small balls of myelin	Degenerated into small balls of myelin
Foot	Small	Small	Normal
Councilman and Dun	Degeneration of myelin in anterior and posterior roots and spinal ganglia		None found
Lehoczky	Small	Some degeneration	—
Neuman, Slauch	Atrophy and increase of connective tissue	..	—
Holmes	Deficient in myelin	Normal	—
Mensi	Small	Small	None found
Rothmann	Small; poor in myelin	Increase in connective tissue; no degeneration	End plate absent; nerve endings normal
Krabbe	Degenerated	Increase in connective tissue	—
Spiller, Silverberg, Lereboullet and Baudoin	Normal	Normal	Normal

and Spiller [17] who, although they found marked pathologic changes in the peripheral nerve, found only ganglion cells decreased in size.

It may be seen from table 6 that the pathologic changes in the muscle are fairly consistent in all cases reported. An increase in the interstitial fat and connective tissue was observed in about half of the cases. Actual degeneration of the muscle was not observed. It was composed of fibers of variable size, for the most part small, with normal striations.

Archangelsky and Abrikosoff [18] found changes in the cord and muscle, but they deem that the pathologic changes in the muscle are

17. Griffith and Spiller: Amyotonia Congenita: A Clinical and Pathological Study, Am. J. M. Sc. **142**:165, 1911.

18. Archangelsky, W., and Abrikosoff, A.: Ein Fall von Myatonia congenita (Oppenheim) mit Autopsie, Arch. f. Kinderh. **56**:101, 1911.

primary. Reuben [19] believes that there is a primary abiotrophy of the muscles in a fetal stage, with secondary failure of the corresponding cells of the anterior horn to develop, due to a deficient natural stimulus from the muscle.

Lehoczky,[15] on the other hand, because the degeneration of ganglion cells in several cases was not limited to the anterior horns, considers that the changes of the cord are primary. He believes the lesion began in fetal life, and that there was a rapid "Abbau," as Spatz [20] experimentally has shown occurs in fetal tissue, which left no phagocytes or scar.

On clinical similarity, Batten [21] at one time considered that amyotonia was a myopathy. The few reports of pathologic changes in the cord found in the myopathies also reveal only a paucity of cells of the anterior horn in these conditions, which has been considered as secondary to the muscular atrophy.

TABLE 6.—*Muscle Changes in Amyotonia Congenita—Twenty-One Cases*

Normal fibers	In all but one case (Kaumheimer's)
Small fibers	In all cases; smallest fibrillae found in Marburg's case
Hypertrophied fibers	Up to 150 microns (Collier and Holmes); absent in six cases
Interstitial fat	Found in all but nine cases
Interstitial connective tissue	Found in all but six cases
Increased sarcolemma nuclei	Found in all but eight cases; round cell infiltration in Foot's case
Longitudinal striations	Diminished in two (Griffith, Councilman and Dun); absent in one case (Spiller)
Cross striations	Diminished in one (Councilman and Dun); absent in four cases (Mensi, Neumann and Baudoin)
Diaphragm	Involved in two cases (Foot, and Wälle and Hotz)
Heart muscle	Involved in one case Lewis)
Blood vessels	Thickened in four cases (Rothmann, Griffith, Marburg and Collier)

Marburg's [13] observations of connective tissue and glial increase with thickening of the blood vessels led him to believe that he was dealing with the end-results of a fetal poliomyelitis. The almost uniform lack of similar observations in other cases makes this theory untenable.

Councilman and Dun [22] consider that there is a toxic action on the nerve endings within the muscle. Holmes [23] believes that there is a developmental defect in the lower motor neuron.

19. Reuben, M.: Amyotonia Congenita of Oppenheim, Arch. Int. Med. **20**: 657 (Nov.) 1917.

20. Spatz, H.: Ueber die Vorgänge nach experimenteller Rückenmarksdurchtrennung mit besonderer Berücksichtigung des Unterschieds der Reactionweise des reifen und des unreifen Gewebes, Nissl- Alzheimer Arb., Erg. Bd., 1921.

21. Batten, F., and Holmes, G.: Progressive Spinal Muscular Atrophy of Infants (Werdnig-Hoffmann Type), Brain **35**:38, 1912.

22. Councilman, W., and Dun, C.: Myatonia Congenita, A Report of a Case with Autopsy, Am. J. Dis. Child. **2**:340 (Nov.) 1911.

23. Holmes, J. B.: Amyotonia Congenita (Oppenheim) Report of a Case with Full Histopathologic Examination, Am. J. Dis. Child. **20**:405 (Nov.) 1920.

Rothmann [12] first suggested that amyotonia is a congenital form of progressive muscular atrophy. Slauch,[24] who reported a case with fibrillation of the muscle fibers, believes that there is a developmental defect of the cells of the anterior horn aided by some exogenous cause such as an acute infection. He quotes Hoffmann, who states: "Amyotonia congenita is not a special form of Werdnig-Hoffmann type of progressive muscular atrophy, it is it itself."

Neumann [25] also believes in the unity of the two conditions and states that the presence of the pyknotic fusiform cells is against the theory of an agenesis, for he believes them to be degenerating cells.

Krabbe [16] combined the cases of amyotonia and Werdnig-Hoffmann type and redivided them into the following two types:

1. Amyotonia: characterized by nonfamilial history, generalized muscular hypotonia, no localized atrophy and clinical improvements. The only cases under this heading which came to necropsy are those of Spiller [2] and Lereboullet and Baudoin,[26] who found no pathologic changes in the cord.

2. Werdnig-Hoffmann Type: heredofamilial, congenital muscle disease, characterized by familial history, localized atrophy and progression. In this group are all of the other cases reported with pathologic changes in the cells of the anterior horn.

Before commenting on these theories it is necessary to review the literature of the Werdnig-Hoffmann type. The literature contains only twenty cases which came to necropsy; they are tabulated in table 7.

As in amyotonia, it is evident that the reports fall naturally into two groups, one in which degenerative changes of the ganglion cells, neuronophagia and changes of the glia cells have taken place, and the other in which there is only a paucity of deformed ganglion cells.

I have therefore combined all of the cases of amyotonia congenita and the Werdnig-Hoffmann type of progressive muscular atrophy in which postmortem examination has been performed without note of the clinical history, in order to reclassify them according to the pathologic changes. This seems justifiable as the sharp differentiation between the two diseases in regard to the onset, familial history, location of atrophy and prognosis does not hold. In a large number of clinical reports abstracted by Faber,[11] generalized hypotonias have been familial and progressive, while localized atrophies have been nonfamilial and

24. Slauch, A.: Ueber Myatonia congenita und infantile progressive spinal Muskelatrophie, Deutsche Ztschr. f. nervenh. **67**:1, 1921.

25. Neumann, P.: Zur pathologische Anatomie der Myatonia congenita, Deutsche Ztschr. f. Nervenh. **71**:95, 1921.

26. Lereboullet and Baudoin: Un cas de myatonie avec autopsie, Bull. et mém. Soc. méd. d. hôp. de Paris **26**:1162, 1909.

the patients have improved. It is only natural to assume that, in spite of the difficulty in clinical differentiation, cases clinically assumed to be one type were so reported when necropsy had been performed, whether the anterior horns revealed a degeneration or a paucity of ganglion cells.

INFANTILE MUSCULAR ATROPHY

1. Werdnig-Hoffmann Type: Degeneration of the ganglion cells with chromatolysis, vacuolization, neuronophagia and glial increase and

TABLE 7.—*Summary of Pathologic Processes in Werdnig-Hoffmann Type*

Hoffmann, case 1	Cells of the anterior horn decreased; many empty cell spaces; chromatolysis of many cells
Hoffmann, case 2	Paucity of ganglion cells; shrunken cells but no neuronophagia; anterior roots atrophic
Hoffmann, case 3	Cells of the anterior horn pale; chromatolysis has occurred, processes degenerated, empty cell spaces, increase in glia; nerve fiber net decreased; degenerated peripheral nerves
Werdnig, case 1	Degeneration of anterior horn; many empty cell spaces; cells rounded, shrunken and indefinitely stained
Werdnig, case 2	Increase in pericellular spaces; definite shrinking, chromatolysis and degeneration of anterior horn cells
Thompson and Bruce	No signs of active degeneration; no fat or pigment in cells; few anterior horn cells
Batten and Holmes	Anterior roots small, poorly stained; paucity of small miniature cells of the anterior horn with normal chromatin; no degeneration
Batten, case 1	Chromatolysis of cells of the anterior horn, marked degeneration of anterior roots and Marchi products present
Batten, case 2	Atrophy of cells of the anterior horn; posterior column degeneration
Batten, case 5	Chromatolysis and atrophy of cells of the anterior horn; degeneration of anterior roots
Batten, case 6	Cells of the anterior horn small and round, poor in chromatin; small anterior roots
Batten, case 7	Chromatolysis of the cells of the anterior horn; marked Marchi degenerative products in anterior roots
Delille and Boudet	Chromatolysis of cells of the anterior horn; anterior roots atrophic
Ritter, case 1 and case 2	Chromatolysis and degeneration of cells of the anterior horn; anterior roots degenerated
Huenekens and Bell	Few normal cells of the anterior horn, others small; no neuronophagia
Duken and Weingartner	Diffuse degeneration of ganglion cells in bulbar nuclei and anterior horns
Parsons and Stanley	Degeneration, fading and chromatolysis of the cells of the anterior horn; no Marchi reaction
Michael	Paucity of cells of the anterior horn; Marchi products in perivasal cells; small shrunken and degenerated cells undergoing chromatolysis
Barton and Ingleby	Few cells of the anterior horn; nuclei pyknotic; vacuolated cytoplasm undergoing chromatolysis; Carke's cells affected

Marchi-staining products of anterior root degeneration. Under this type are included the cases of Marburg,[13] Kaumheimer,[14] Foot,[5] Wälle and Holtz,[6] Lehoczky,[15] Krabbe,[16] Hoffmann [27] (two cases), Werdnig [28]

27. Hoffmann, J.: Ueber chronische spinale Muskelatrophie im Kindesalter auf familiäre Basis, Deutsche Ztschr. f. Nervenh. **3**:427, 1893; Weitere Beitrag zur Lehre von den hereditären progressiven spinalen Muskelatrophie im Kindesalter, ibid. **10**:292, 1897; Dritter Beitrag zur Lehre von den hereditären progressiven spinalen Muskelatrophie im Kindesalter, ibid. **18**:217, 1900.

28. Werdnig, G.: Zwei frühinfantile hereditäre Fälle von progressiven Muskelatrophie unter dem Bilder der Dystrophie aber auf neurotischer Grundlage, Arch. f. Psychiat. **22**:437, 1890; Die frühinfantile progressive spinalen Amyatrophie, ibid. **26**:706, 1894.

(two cases), Parsons and Stanley,[29] Batten [21] (cases 1, 2, 5 and 7), Delille and Boudet,[30] Michael,[31] Barton and Ingleby,[32] Dunken and Weingartner,[33] and Ritter [34] (two cases).

2. Oppenheim Type: A paucity of cells of the anterior horn and the presence of abnormal cell types without signs of degeneration. Under this type fall the cases of Hoffmann (two cases), Thomson and Bruce,[35] Batten,[21] Beevor,[36] de Villa,[37] Huenekens and Bell,[38] Baudoin,[10] Holmes,[23] Silverberg,[39] Griffith and Spiller,[17] Archangelsky and Abrisokoff,[18] Collier and Holmes,[3] Slauck,[24] Neumann,[25] Concetti,[11] Mensi,[11] Rothmann,[12] Mettenheimer,[40] Spiller,[2] and Lereboullet and Baudoin.[26]

The clinical significance of this classification is not great, for the groups clinically merge and combine with each other, as previously stated. The selective site of the pathologic changes is exactly the same, and these changes in the muscles of the two types are identical. The difference is found only in the cells of the anterior horn.

In one the process is completed or stationary. The few ganglion cells present are deformed and some are hypertrophied, which suggests a fetal process. Products of degeneration are lacking, probably because the process had run its course when the tissue was fetal. Just as in other congenital diseases, it is impossible to state definitely whether a developmental defect or a fetal degeneration is the fundamental process.

29. Parsons, L., and Stanley, D.: Progressive Spinal Muscle Atrophy of Young Children (Werdnig-Hoffmann Type): Report of a Case with Pathological Examination, Brain **35**:50, 1912.

30. Delille, A., and Boudet: Les lésions anatomiques de l'amyotrophie spinale diffuse des nouveaux nés, Arch de méd. d. enf. **11**:32, 1908.

31. Michael, J.: Infantile Progressive Muscular Atrophy of Werdnig Hoffmann Type, Arch. Neurol. & Psychiat. **9**:582 (May) 1923.

32. Barton, E. A., and Ingleby, H.: A Case of Werdnig-Hoffmann Paralysis, Lancet **2**:922, 1919.

33. Duken, J., and Weingartner, A.: Klinischer und pathologisch-anatomischer Befund bei einen Fall von frühinfantilen progressiven spinalen Muskelatrophie (Werdnig-Hoffmann), Ztschr. f. Kinderh. **29**:245, 1921.

34. Ritter, L.: Zur Kenntnis der progressiven spinalen Muskelatrophie im frühen Kindesalter, Jahrb. d. Kinderh. **59**:224, 1904.

35. Thomson, J., and Bruce, A.: A Case of Progressive Muscle Atrophy in a Child with a Spinal Lesion, Edinburgh Hosp. Rep. **1**:361, 1893.

36. Beevor, C.: A Case of Congenital Spinal Muscle Atrophy (Family Type), Brain **25**:85, 1902.

37. De Villa: Arch de méd. d. enf. **19**:137, 1911. Cited by Reuben (footnote 19).

38. Huenekens, E., and Bell, E.: Infantile Spinal Progressive Muscular Atrophy (Werdnig and Hoffmann Type), Am. J. Dis. Child. **20**:496 (Dec.) 1920.

39. Silverberg, M.: Ueber die pathologische Anatomie der Myatonia congenita und die Muskeldystrophien im allegemein, Virchows Arch. f. path. Anat. **242**:42, 1923.

40. Mettenheimer: Myatonia congenita, abstr., Neurol. Centralbl. **34**:655, 1915.

In the second group, degeneration of the ganglion cells was in active process. From this, one may conclude that the process of degeneration began later or that it proceeded more slowly. In all other respects the pathologic changes in the two groups are the same.

CONCLUSIONS

A pathologic study of a case of amyotonia congenita and a review of the published necropsy reports on amyotonia congenita and the Werdnig-Hoffmann type of progressive muscular atrophy shows that in these diseases two groups of cases may be determined. These groups are identical as far as the pathologic changes in the muscle and the location of the changes are concerned, but differ as to the type of lesion in the cord. In one a paucity of cells of the anterior horn with the presence of abnormal cells is found; in the other actual degeneration of the ganglion cell and neuronophagia. It is not possible in the first group to determine whether the process is a developmental defect or a degeneration. The fundamental difference in the two groups is probably only a matter of the time at which the ganglion cells are affected.

All the infantile degenerative muscular atrophies may be classed according to this pathologic criterion, the first called type Oppenheim, the second, type Werdnig-Hoffmann. There is no definite clinical differentiation between them, each type merging into the other.

DISCUSSION

DR. PETER BASSOE: I regret that I have no observations to offer. I have seen a few cases that probably were of this type, but no anatomic investigation has been made. The Werdnig-Hoffmann type is rare, and I should like to know how many physicians are sure they have seen a case. I have seen one case that I am sure was of the Werdnig-Hoffmann type. The contrast is striking; the child with the Werdnig-Hoffmann type is very sick, which is not always true of the child with amyotonia congenita. The latter condition is compatible with good general health. From a study of the literature at that time, I learned that there is something malignant about the Werdnig-Hoffmann disease. The prognosis is extremely unfavorable. The children never straightened out as those with amyotonia congenita do. In the Werdnig-Hoffmann type of cases one always gets a definite history that the baby was normal, and that the trouble began at the age of 6, 7 or 8 months. I would be slow in making a diagnosis of amyotonia congenita unless the evidence showed that the baby had always been deficient in motor power. Some of the cases reported as amyotonia congenita probably were cases of Werdnig-Hoffmann atrophy, as even many neurologists are not familiar with the latter condition.

DR. JULIUS GRINKER: I have seen a case of the Werdnig-Hoffmann type of progressive muscular atrophy and also a typical case of amyotonia congenita, and they were exactly as Dr. Bassoe stated. In the case of amyotonia congenita the patient has never been able to use his muscles, but otherwise is in good health. Furthermore, I have noticed that there has been definite improvement. The patient of the Werdnig-Hoffmann type of case has not improved,

as far as I know. I believe that the pathologic anatomy in these two similar conditions explains why a patient with one condition should improve and a patient with the other condition should have progressive symptoms.

DR. ROY GRINKER: It was interesting to me to hear clinical evidence that the Werdnig-Hoffmann type of a case means that the child is sick with progressive symptoms, and that in amyotonia the patients improve. The difficulty with the reports in the literature has been that there have not been enough cases in which the pathologic changes have been described to classify them in one or the other group. Therefore, many cases which were clinically described as amyotonia congenita were pathologically accepted as amyotonia congenita, but in reality were of the Werdnig-Hoffmann type. The statement that amyotonia congenita is usually present at birth is borne out by pathologic observations, but here the point I mention is the reason why cases have been reported in which amyotonia congenita supposedly developed in the first or second year, when in reality they were of the Werdnig-Hoffmann type.

An interesting thing in regard to the chemical changes in these patients is that, in cases of atrophy, whether it is progressive muscular atrophy, amyotonia congenita, the Werdnig-Hoffmann type or even myasthenia, there is a low creatinine and a high creatine output on a low protein diet. The significance of this altered chemical change is not known. Perhaps it is secondary to muscular inactivity.

STUDIES IN STUTTERING

II. PHOTOGRAPHIC STUDIES OF THE VOICE IN STUTTERING*

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IOWA CITY

A previous paper [1] has suggested the value of study of the stutterer's voice and speech by means of the photographic method. It also indicated the desirability of contrasting objective records of different kinds of speech, such as emotional and unemotional, repetitive and propositional and the several combinations of these varieties. In this paper, I shall report a study of emotional and unemotional repetitive speech and unemotional propositional speech. On several occasions, the voice and the breath stream were photographed during the act of stuttering, and these records furnished interesting additional data for study.

Methods of photographing the voice have been well worked out in the Psychology Laboratory of the University of Iowa and are fully reported by Herzberg,[2] Kwahlwasser,[3] Simon [4] and Metfessel.[5] Briefly, Dorsey phonelescopes are used as optical levers for recording both the sound waves of the voice and the 100 double vibration tuning fork. The records are made on Eastman superspeed, standard size motion picture film and show in the majority of instances three lines—a base line, a time line and a voice line. Pitch is read by counting the number of vibrations from the voice that occur within a hundredth of a second. This number is multiplied by 100 to give the number of vibrations per second. Duration of tone is computed by counting the number of 0.01 second-distances occupied.

Unemotional repetitive speech was obtained by having the subject repeat a sentence he had previously memorized, which was as free from emotional coloring as possible. Emotional repetitive speech was secured

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* The work here recorded was carried out in the laboratories of the Iowa State Psychopathic Hospital as part of the program of research in physiology of the brain which is being supported by a grant from the Rockefeller Foundation. Additional funds have also been supplied by the Graduate College of the State University of Iowa.

1. Travis, L. E.: A Phono-Photographic Study of the Stutterer's Voice and Speech, Iowa Studies in Psychol., Psychological Monographs **36**:109, 1926.

2. Herzberg, A. A.: Photography and Interpretation of a Vocal Rendition of Annie Laurie, Thesis, University of Iowa, 1923.

3. Kwahlwasser, Jacob: The Vibrato, University of Iowa Studies in Psychology, 1926, no. 9.

4. Simon, Clarence: The Variability of Consecutive Wave Lengths in Vocal and Instrumental Sounds, University of Iowa Studies in Psychology, 1926, no. 9.

5. Metfessel, Milton: Technique for Objective Studies of the Vocal Art, University of Iowa Studies in Psychology, 1926, no. 9.

by requiring the subject to repeat, after the experimenter, a sentence that carried a personal reference of high emotional value. The individual had no knowledge of the sentence until he was asked to repeat it for photographic purposes. Unemotional propositional speech was secured by having the subject discuss some topic with which he was known to be familiar. This always concerned some phase of school work.

Twenty stutterers and an equal number of nonstutterers served in this study. Two or three from each group were graduate students, the remainder being undergraduates.

Studies carried on by Schoen,[6] Herzberg,[2] Metfessel[5] and Kwahlwasser[3] have shown that when a tone is sustained during artistic singing, the pitch is not held constant but fluctuates at an average variation of one tenth of a tone above and below its mean. This fluctuation takes place at a rate of from 4 to 9 per second and has been called the vibrato. Fluctuations much beyond this range of pitch variation constitute a tremolo. Gray,[7] in a study that dealt chiefly with emotional repetitive speech, found the vibrato to occur in about 83 per cent of normal persons. From a personal familiarity with his technic and subject material, I am of the opinion that the majority, if not all, of his records which show the vibrato were produced during intonation and not in the course of natural fluent speech. This factor of intoning and the emotional factor make his results such that they cannot be compared with those from unemotional conversational speech. According to my experiments, the vibrato occurs in a certain number of the stutterer's tones during unemotional conversational speech, and in the case of the nonstutterer it does not occur in any tones of similar speech.

STUDIES BY THE GRAPHIC METHOD

Figure 1 shows graphs of a number of speech tones of the stutterer having the typical vibrato of about six pulsations a second. Figure 2 presents graphs of typical speech tones of the nonstutterer which do not give any indication of the vibrato. Figure 3 shows a stutterer's tone which furnishes two pulsations at the rate of about six a second and five pulsations at the rate of approximately ten a second. The latter pulsations are followed by extreme tonal fixation.

In figure 4, the stutterer's voice gives two pulsations of extremely large variation in pitch. The pitch fluctuations were several times as large as those found in the typical vibrato, and this sounded like a tremolo. Figure 5 shows varying degrees of tonal fixation in the case

6. Schoen, Max: Pitch Factors in Artistic Singing, University of Iowa Studies in Psychology, 1922, no. 8.

7. Gray, G. W.: The Vibrato in Speech, Quart. J. Speech, 1926, ed. 12.

of the stutterer's unemotional conversational speech. Figure 6 is a single tone from the stutterer's speech. It lasted slightly more than six seconds. The patient was saying "I" in an attempt to begin a sentence. This tone presents both the typical vibrato and the exaggerated vibrato or tremolo The tremolo has superimposed on it pulsations at the rate of about 25 a second which also occur two or three other times during the tone. There is a marked fluctuation in pitch occurring four times during the sound. It almost reaches D# in the first two pulsa-

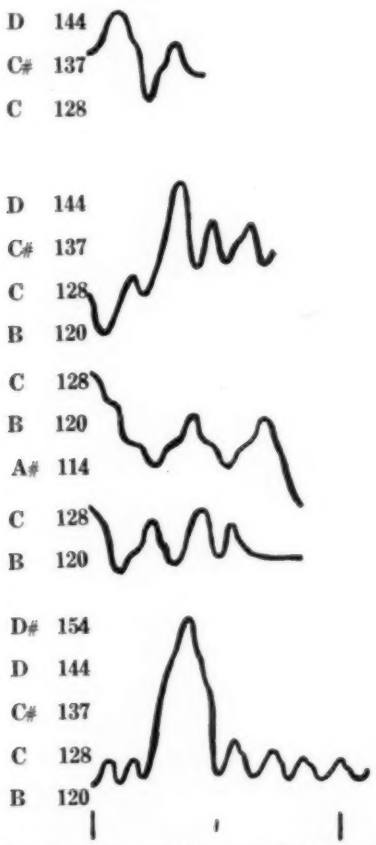

Fig. 1.—Tones of the stutterer during unemotional propositional speech. In these and all subsequent graphs of tones, the ordinate scale gives pitch and the abscissa, duration. Time is indicated in seconds and half seconds.

tions, E in the third and F# in the fourth. The ending of the tone is unusual in that the change in pitch extends from a point about midway between C and C# to almost F#, and from F# it falls practically to C#. This excursion occupies about 0.6 of a second.

The vibrato is probably the result of clonic contractions in the muscles responsible for voice production. Periodic fluctuations in

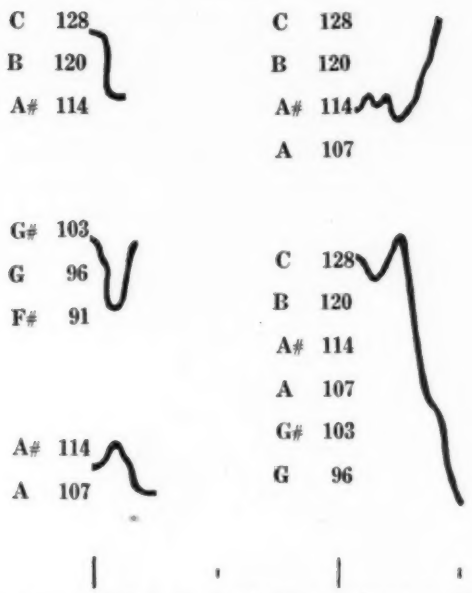

Fig. 2.—Tones of a normal person during unemotional propositional speech.

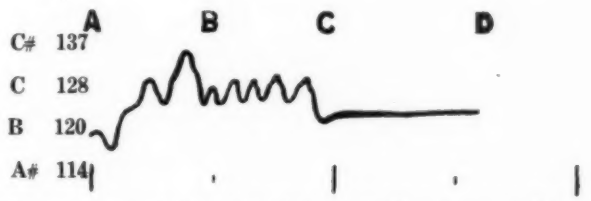

Fig. 3.—Tone of the stutterer during unemotional propositional speech.

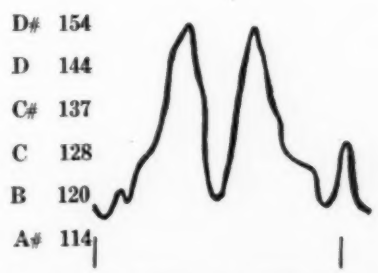

Fig. 4.—Tone of the stutterer during unemotional propositional speech.

pitch, such as are presented by the vibrato, must result from periodic fluctuations in the tension of the vocal cords, and three possible explanations of such changes in tension suggest themselves: they might result from variations in the action of certain of the intrinsic muscles of the larynx; they might follow changes in the breath pressure with or without active changes in tension of the vocal cords; they might result from

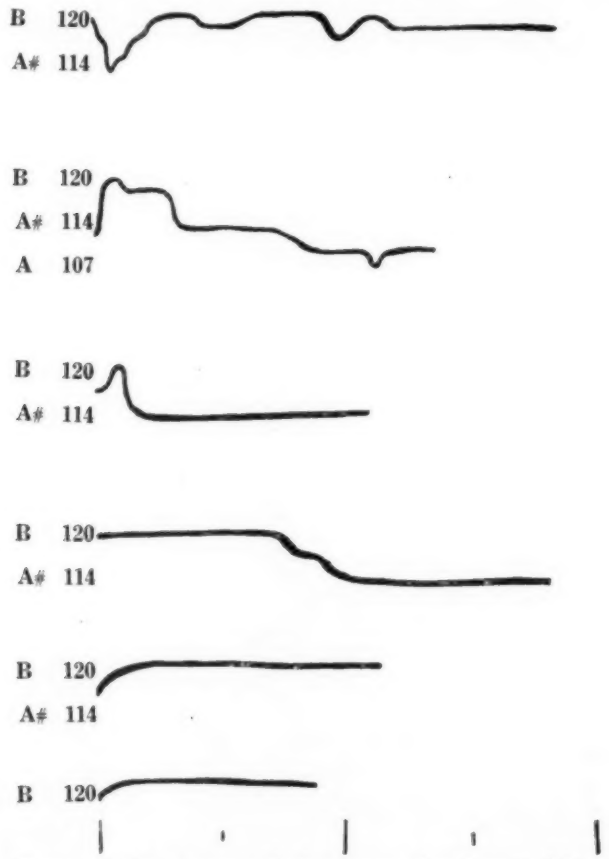

Fig. 5.—Tones of the stutterer during unemotional propositional speech.

action of the extrinsic muscles of the larynx which serves to elevate it for the production of high notes and depress it for low notes.

Seashore and his students have found that the vibrato is characteristic of singing tones and that the tone which lacks it is of a quality that, other things being equal, is less pleasing. It does not occur in normal speech tones in casual conversation, which characteristically lacks sustained effort in the production of any one sound. The stutterer, on the other hand, displays great effort in sound production and certain patients prolong to a remarkable extent each vocalization and thus pre-

sent the two conditions that are commonly associated with the appearance of the vibrato.

Figure 3 presents a series of occurrences that are suggestive. The tone really consists of three parts. Part one (*A* to *B*) has two pulsations at the rate of 6 per second, which is about that of the vibrato; part two (*B* to *C*) has five pulsations at a much more rapid rate, 10 or 12 per second; part three (*C* to *D*) appears as prolonged tonal fixation. There is here a striking suggestion of progression through clonus into spasm such as that recorded by Cobb [8] in the transition from clonic reflex movements into tetanic contractions.

This figure serves as a bridge to span the gap between tones showing the vibrato and those exhibiting tonal fixation. Tones presenting the latter characteristic vary considerably from each other and present various degrees of pitch fixation.

The first and second of the stutterer's tones, as given in figure 5, bear some resemblance to those of the nonstutterer in that they show pitch

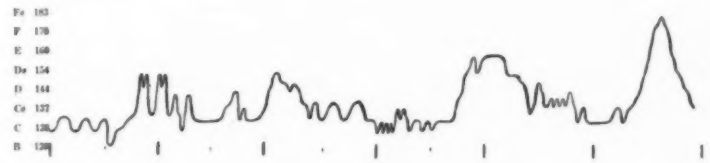

Fig. 6.—Tone of the stutterer during unemotional propositional speech.

variations of an aperiodic nature. The periods of tonal fixation, however, are much longer than any found in normal tones and the tones as a whole have more than twice the duration that the longest of the normal tones show. The remainder of the tones show a remarkable degree of tonal fixation. The extreme lack of pitch variation in the third tone is relieved at the beginning, while there occurs a gliding effect about the middle of the fourth tone. To have a variation in pitch occur at the beginning of a speech sound is probably typical, and in this particular respect the first, second and third tones are not unusual. In the third tone after the single initial excursion, no other variation occurred throughout the remaining one second. The last two tones are atypical not only in regard to extreme pitch fixation but also in that they show little of the usual initial variation in pitch.

The variation in pitch which is characteristic of the normal tone indicates that in the normal person there occur alterations of the fixed muscular tension which would be requisite for the maintenance of a tone of absolutely constant pitch. The absence of such variations, therefore,

8. Cobb, Stanley: Electromyographic Studies of Tonus, Bull. Johns Hopkins Hosp. **29**:247. 1918.

especially for any appreciable length of time, is to be considered as abnormal. The abnormality would seem to consist of marked fixation on the part of those muscles that have to do with altering the tension of the vocal cords, so that the muscular balance necessary for tone production is for some reason or other maintained in a condition of rigidity that is pathologic.

It is difficult to give an adequate interpretation of the tone presented in figure 6. This tone shows all the abnormalities found in the various sounds previously considered. The duration which seems to be unusual in the case of practically all the stutterer's tones is here extreme. It is all the more remarkable when it is considered that the stutterer was really trying to release the tone in a desire to start a sentence. From an extensive observation of this particular individual, I am fairly certain that each of the four large excursions in pitch represents periods of increased effort.

The graphs of the tones of nonstutterers need little comment. They present the usual variation in pitch of an aperiodic type. Neither the vibrato nor tonal fixation is found in any of the figures.

A more detailed study of duration of tones during unemotional conversational speech reveals some further interesting differences between those of the stutterer and the normal.

One of the severer cases of stuttering and a normal person who has an approximately average rate of speed in speaking furnished the records for comparison. The duration of fifty consecutive tones was determined from each record, and the results are presented in the accompanying table.

Range, Mean and Standard Deviation for Duration of Tones

Subject	Range	Mean Duration (Seconds)	Standard Deviation (Second)
Stutterer	0.1 to 6.1 seconds	1.43	0.17
Normal	0.1 to 1.3 seconds	0.49	0.04
	Observed differences	0.94	0.13
	Probable error	±0.016	±0.011

The difference between the mean durations and the difference between the standard deviations are both so much larger than their respective probable errors that they are significant. Thus on the average the stutterer holds his tones almost three times as long as the normal. On the other hand he shows greater variation in the length of time he holds his tones, as is indicated by the standard deviation and the range. The stutterer varies between 0.1 of a second and 6.1 seconds, while the nonstutterer varies between 0.1 and 1.3 seconds. Figure 7 shows the distribution curves for duration of tones from the material used in constructing the table.

To find these marked differences between stutterers and nonstutterers in duration of speech tones is, after all, not surprising. The same factors that are responsible for the stutterer's inability to begin a sound would seem to express itself in the initiation of the subsequent sound.

DATA OBTAINED FROM ORIGINAL PHOTOGRAPHS

The material so far presented has been derived by constructing graphs from phonelescope records of the voices of stutterers and of normal persons. Some additional factors of interest may be observed in the original photographs.

One of these is a periodic fluctuation of breath pressure of slight amplitude and long period which is apparent in many films just before, between and immediately after tones in speaking (figs. 8 and 9). These waves are shown by the approach of the voice curve to the base line

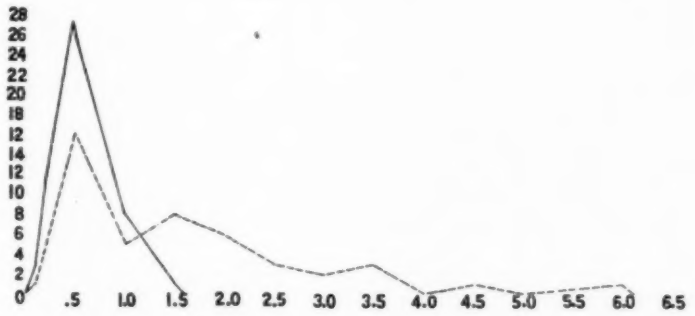

Fig. 7.—Distributions for duration of tones for a stutterer and a normal person during unemotional propositional speech. The ordinate scale gives the number and the abscissa, the duration of tones. Duration is indicated in terms of seconds and half seconds. The solid line indicates the normal voice, and the broken line, that of the stutterer.

directly below the points marked *A, B, C,* etc. They occur at a rate varying between 25 and 50 per second. Following the observation of this phenomenon, Metfessel [9] has found certain of his records of singers' voices to present the same fluctuations. The same periodic fluctuations of about the same amplitude and period can be seen in figure 10, but here they are complicated by a shorter wave which in period is not unlike a voice wave whose amplitude is so small that it probably is not audible; no vocalization was noted by the examiner at the time of their production. The large waves are indicated by letters as in figures 8 and 9. Of twenty stutterers, ten showed this phenomenon, while of the same number of nonstutterers only one gave such a record; this occurred on only one occasion, during emotional,

9. Personal communication to the author.

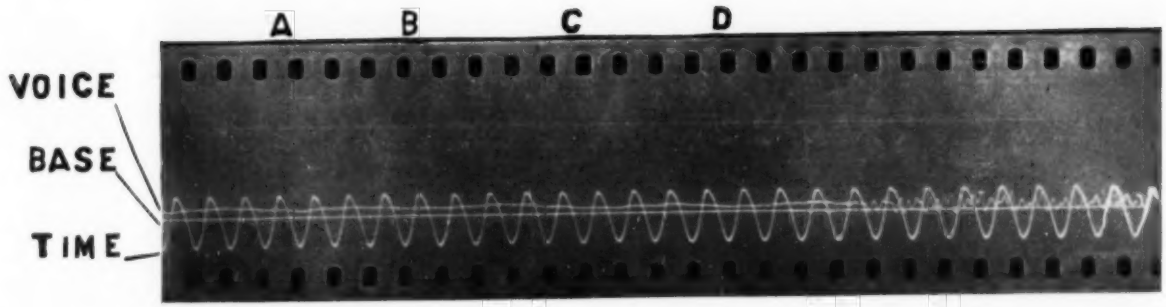

Fig. 8.—Pulsations in the breath stream (voice curve) of a stutterer before the initiation of a tone in unemotional repetitive speech. No observable signs of stuttering were noted. In this and all subsequent pictures, time is indicated in hundredths of a second.

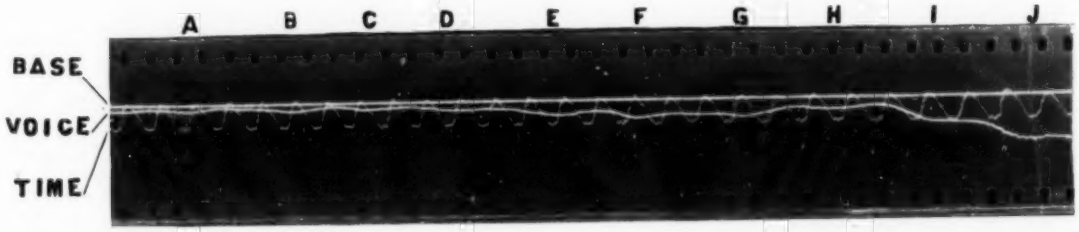

Fig. 9.—Pulsations in the breath stream (voice curve) of a stutterer during stuttering in unemotional propositional speech.

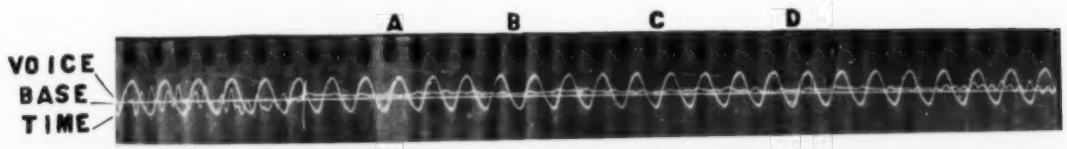

Fig. 10.—Pulsations in the breath stream (voice curve) complicated by shorter waves not unlike voice waves in unemotional repetitive speech in the stutterer. No indications of stuttering were observed.

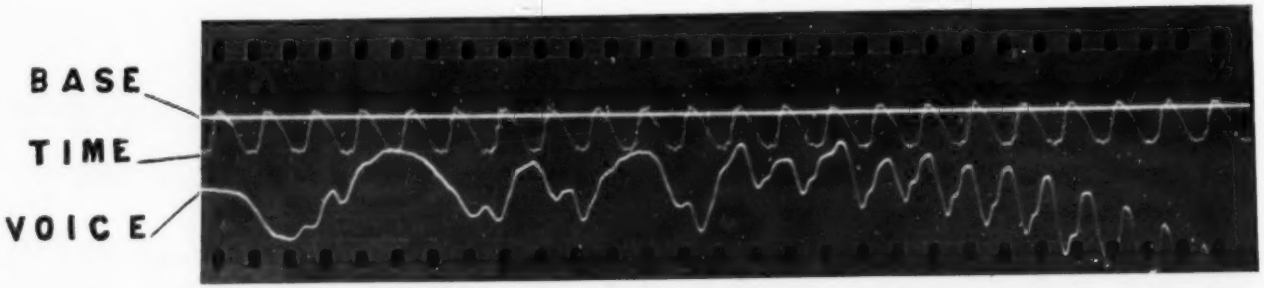

Fig. 11.—Marked variation in length of consecutive waves in a voice record of a stutterer in unemotional propositional speech. Evidences of disturbances in speech were noted.

repetitive speech. Hill [10] recorded tremors in voluntary muscular contraction at a rate of 40 or 50 per second, which thus corresponds with this rate of pulsation in the outgoing breath stream of the stutterer during speech.

It should be noted that these pulsations occur both during stuttering and when there are no observable evidences of difficulty in speaking and hence are to be considered as not characteristic of the act of stuttering alone; they furnish an apparent difference between the free speech of the stutterer and that of the normal.

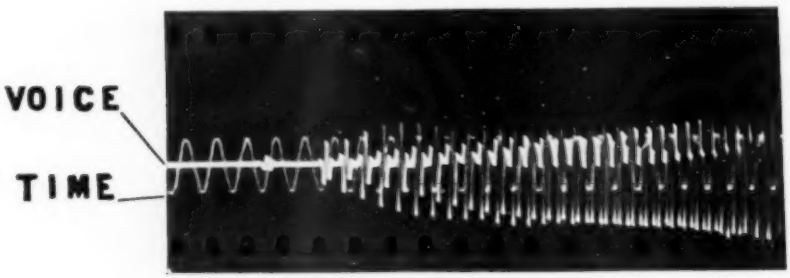

Fig. 12.—Two double vibrations about 0.02 seconds before the voice wave begins. Emotional repetitive speech of a stutterer. No evidences of difficulty in speaking were noted.

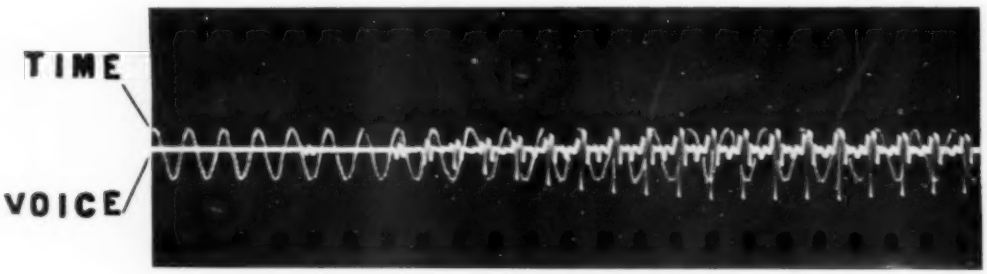

Fig. 13.—Two double vibrations approximately 0.04 seconds before the voice wave appears. Emotional repetitive speech of a stutterer. No difficulty in speaking was evident.

Figure 11 is a record of a stutterer made during casual conversational speech. Records of waves of this bizarre form have been obtained many times in photographs of the voice in this particular case but have not been encountered in other stutterers. The three large waves are not of the same length. The first complete one occupies approximately 1/25 of a second; the second, 1/50 and the third, 1/40. The next two

10. Hill, A. V.: The Tetanic Nature of Voluntary Contraction in Man, Proc. Physiological Soc., March 12, 1921, xiv-xvi; J. Physiol. **5**:133, 1921.

waves occupy 1/100 of a second each, while the next occupies 1/75. From here on, the waves occur regularly at about 95 per second. The length of the sixth wave as compared with the two preceding it and with those following would seem to indicate a recurrence of the factor which modified the first three. I have examined photographic records of many thousands of sounds, and such large differences in duration of consecutive waves have never been observed in the speaking and singing tones of normal voices.

We have as yet no concise information as to whether these unusual waves are due to spasmodic action of the glottis, marked changes in breath pressure or large alterations in the tension of the vocal cords.

In the speech records of many of our stutterers, there occur two double vibrations before the voice waves proper begin (figs. 12 and 13). The length of time elapsing between the double vibrations and the appearance of voice waves varies in different cases and for the same individual at different times. It, rarely, if ever, exceeds 0.04 second. There seems to be another variety of this phenomenon in the photographs of the voices of certain stutterers which show four or five vibration couplets about 1/6 second before the voice wave. This is presented in figures 14 and 15. In the first record there occur five short periods of vibrations followed by an interval of quiet of approximately 0.16 seconds, and in the second a number of such vibrations occurs between the two tones that are recorded by the waves at either end of the figure. This phenomenon has been frequently encountered before tones, and it has never been found following a tone unless its occurrence between tones, as in figure 15, is to be interpreted as following the first rather than anticipating the second.

The voice records in two of the severer cases show consistently larger groups of oscillations of high frequency but low amplitude, which occur periodically at a rate of approximately 16 per second between tones or after a tone in unemotional propositional speech (fig. 16). These have never been observed to precede the voice waves of the first tone of a sentence. They seem, therefore, to be related to cessation rather than to initiation of voice. The rate of the oscillations within the groups varies between 500 and 900 per second.

This phenomenon, although it is best seen on an outgoing breath stream of medium intensity, is present during both inspiration and expiration even when the passage of air is rapid. Figure 17 shows that the relatively sudden expiration does not interrupt these oscillations that are recorded at the usual intervals of 0.06 second. Figure 18 presents a good example of strong inspiration following the cessation of a tone, and the groups of small oscillations are to be seen at the initiation of inspiration and during the entire inspiratory period.

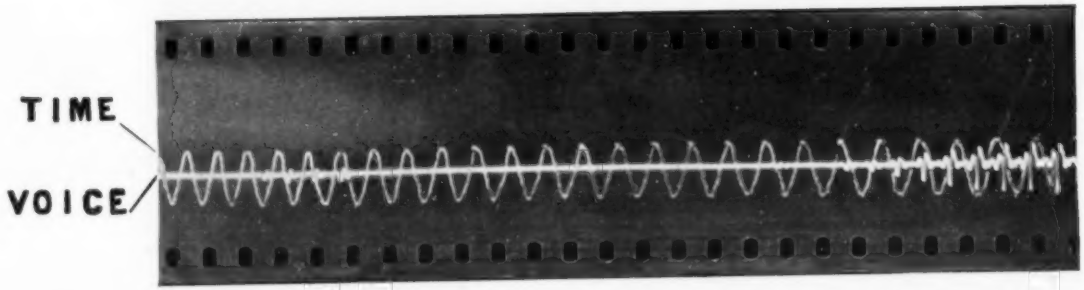

Fig. 14.—A group of vibrations of low amplitude occurring about 0.16 seconds before the voice waves begin. Emotional repetitive speech of a stutterer. No indications of stuttering were noted.

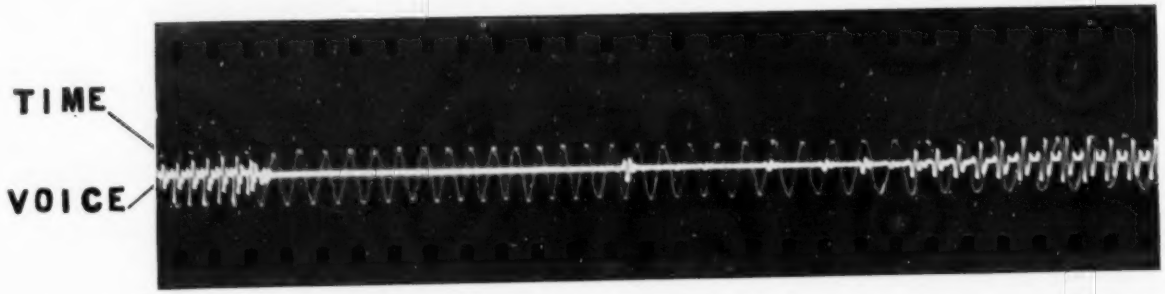

Fig. 15.—Double vibrations between tones in emotional repetitive speech of a stutterer. No stuttering was noted.

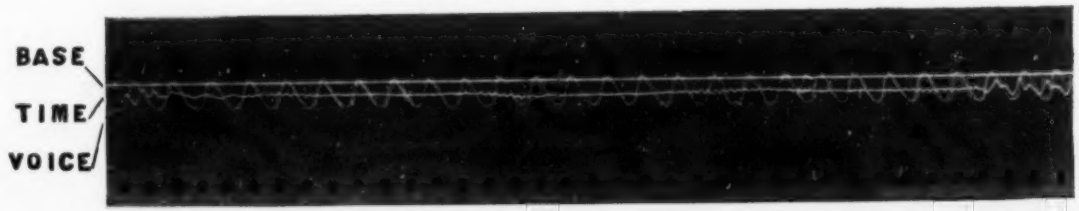

Fig. 16.—Groups of oscillations of high frequency but low amplitude occurring periodically at a rate of about 16 per second between tones in unemotional propositional speech of a stutterer. No signs of stuttering were noted.

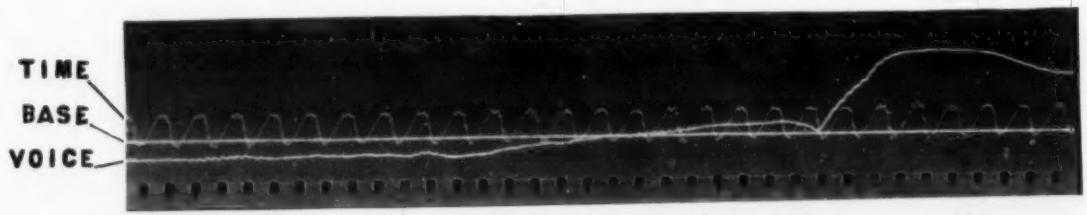

Fig. 17.—Several groups of oscillations of high frequency but low amplitude, one of which occurs during a rather sudden expiration which is indicated by an upward movement of the voice line. Unemotional propositional speech of a stutterer. Slight signs of stuttering were noted.

Fig. 18.—Groups of oscillations of high frequency but low amplitude appearing during a strong inspiration at a rate of about 16 per second. Unemotional propositional speech of a stutterer. Inspiration is indicated by a downward movement of the voice line after the termination of the voice waves. No signs of difficulty in speaking were noted.

Fig. 19.—A series of oscillations at about 500 per second which is initiated extremely suddenly by a wave of much greater amplitude than any of its followers. The group of oscillations of high frequency but low amplitude appear periodically later in the record. Unemotional propositional speech of a stutterer.

In figure 19 there occurs, without previous vocalization, a long series of oscillations at approximately 500 per second which is initiated by waves of much greater amplitude but of about the same frequency. These oscillations begin abruptly and continue uninterruptedly for approximately 0.12 second. After a quiet period of 0.03 second, they occur periodically in groups of about 10 or 12 oscillations.

There are two other peculiarities about this curve: first, the extreme suddenness with which the vibrations begin, and second, the amplitude of the first wave, which is twice that of any of its followers. In the normal speech tone (fig. 20), there is a more or less gradual building up until the maximum is reached at about the fourth wave.

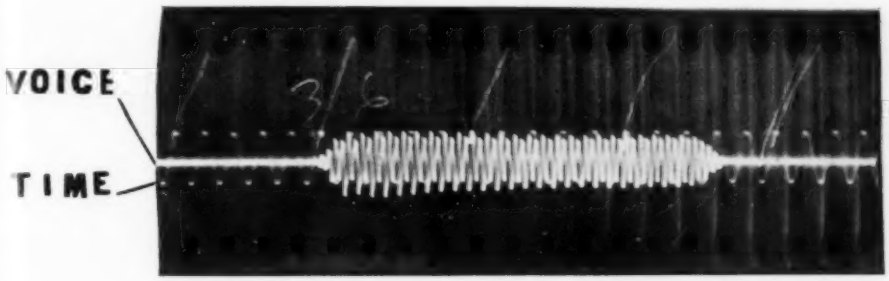

Fig. 20.—Voice record in normal emotional repetitive speech.

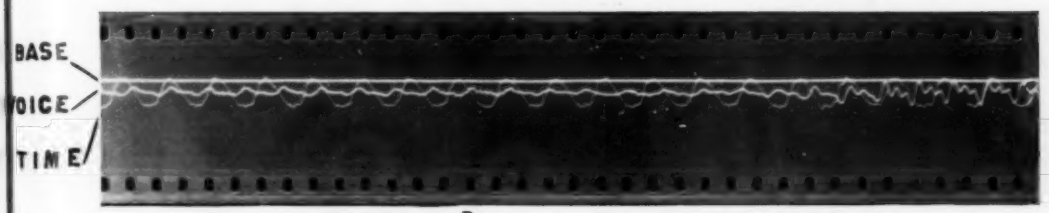

Fig. 21.—Two groups of oscillations of high frequency but low amplitude occurring periodically at a rate of about 16 per second during vocalization in unemotional propositional speech of a stutterer. One group appears above the point marked *A* and the other above the point marked *B*. No signs of stuttering were noted.

Similar groups of small oscillations of high frequency but low amplitude may be observed to occur during vocalization. In figure 21, one group appears above the point marked *A* and another above the point marked *B*.

SUMMARY

Photographic records of the stutterer's voice in unemotional, propositional speech show the following: (1) the presence of a vibrato and tremolo; (2) periods of tonal fixation, and (3) marked prolongation of

tones. In all three types of speech studied (emotional and unemotional repetitive and unemotional propositional) the photographs show: (1) periodic fluctuation of breath pressure before, between and after tones, and (2) short periods of vibrations before the voice waves proper begin. Some of these phenomena were found in every stutterer studied and all were encountered frequently. In addition, certain cases showed in unemotional propositional speech: (1) bizarre waves in the voice curve which present marked variation in length: (2) groups of oscillations of high frequency but low amplitude at a rate of approximately 16 per second between tones, after a tone or during vocalization and (3) long series of oscillations at about 500 per second which are initiated extremely suddenly by a wave of much greater amplitude than any of its followers. None of these records are common in photographs of the voice in normal speech.

THE FANTASY OF NOT BELONGING TO ONE'S FAMILY*

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NEW YORK

Modern psychiatry stresses the importance of studying in detail the mental content. The delusions of psychoses, the symptoms of neuroses and many conduct disorders are more intelligible when the fantasy life of the patient is investigated. Not all fantasies are pathologic. Indeed, for the maintenance of mental health a certain degree of fantasy is essential. From its roots plans are formed, and acts result if nurtured in the atmosphere of reality. However, normal fantasy becomes abnormal when uninfluenced by reality, as indicated in this study of the fantasy of not belonging to one's family, which finds expression not only in the malignant but in the benign mental disorders as well as in the borderline group.

Patients who come for analysis frequently volunteer, not without some hesitation, the fantasy, in one form or another of not belonging to the family. The information is imparted falteringly, and they attempt to conceal embarrassment by joking about it. In this manner the ambivalence toward the fantasy is shown—the unconscious belief in its truth and the conscious criticism of its absurdity. On being questioned, patients rarely can give the exact onset of the fantasy except to say that they seem to have had the feeling "of not belonging to the family" as far back as they can remember. Some will state that in childhood a remark of a female relative led them to infer their illegitimacy, the secret of which had never been betrayed to any one else. Others will give as the reason for the fantasy a lack of resemblance to the rest of the family. A difference in the color of the eyes, in the shade of the hair or in the shape of the nose may be the basis for the suspicion.

When attention is given to the form of the fantasy, it is found that it expresses itself in several variations. Not always is the patient alone concerned, but his sister, brother or offspring may be fantasied as being illegitimate. Others will disguise the fantasy by regarding themselves as an hereditary accident—a sort of mendelian recessive or dominant

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* Read before the Ward's Island Psychiatrical Society, in conjunction with the presentation of suitable cases by Dr. Sarah R. Kelman, Oct. 27, 1926.

character. Depending on the theme of the fantasy, I have tentatively made the following groups: (1) the fantasy of illegitimacy: (*a*) one's own, (*b*) one's sister or brother, (*c*) one's offspring; (2) the fantasy of having been adopted (foster parentage); (3) the fantasy of royal lineage; (4) the fantasy of savage lineage.

Except in the psychoses, the idea of illegitimacy is generally recognized by the patient as a fantasy. But his conduct at home and at school and his social relationships betray its unconscious validity. Everywhere, his behavior is that of one who does not belong, and he may feel superior or inferior to those with whom he associates. When the fantasy relates to a brother, sister or child, it is not recognized as such. Interestingly enough, the object of the fantasy receives more than his share of affection from the patient, thus betraying the mechanism of identification. The doubt of the legitimacy of one's offspring is common in everyday life, and many writers of fiction and drama have availed themselves of this theme. Strindberg's "Father," Maupassant's "Pierre et Jean," Ibsen's "Wild Duck" and Shaw's "Candida" are only a few of the many examples in literature in which the idea of not belonging to the family is the choice theme.

The fantasies of foster parentage and royal lineage are most frequently evidenced in delusions. The idea of being a crown prince deprived of his heritage, as well as poses of exaltation, is a common occurrence in mental illness. Thus a patient at Manhattan State Hospital gave the following account of his birth: "The woman that I knew as my mother made a death-bed confession saying that I was not her child, that the mother who brought me into the world was a Scotch girl, a Scotch princess. She was the grand-daughter of King George III of Scotland. She was also the daughter of the man known in the history of the Irish as the Lord Edward Fitzgerald. That was my real murdered mother, the mother that I have never seen, the mother that I have never laid my eyes on. It is as true as the Almighty God in heaven. I solemnly swear that my real murdered mother is the daughter of the Lord Edward Fitzgerald." Imposters and poseurs are dominated by this fantasy unconsciously. National upheavals such as the Russian revolution are taken advantage of for the release of this fantasy in various forms. Many Russians who are cabmen in Paris claim to be descendents of royalty, and many immigrants speak of the social position and estates that their family once had in the country of their birth. In mythology, Rank [1] has pointed out the uniformly common theme of the Birth of the Hero, and from the various myths has constructed a standard saga. The schedule is that the hero is the child of most dis-

1. Rank, Otto: The Myth of the Birth of the Hero, New York, Nervous and Mental Disease Publishing Company, 1914.

tinguished parents, usually the son of a king. His origin is preceded by difficulties, such as continence or sterility due to prohibitions or other obstacles. During the pregnancy, there is a prophesy, in the form of a dream or oracle, cautioning against his birth and threatening danger to the father. The hero at birth is surrendered to the water in a box, or placed in a cave. He is then saved by lowly people and suckled by a lowly woman or a female animal.[2] After the hero grows up, he finds his distinguished parents and finally achieves an exalted position and honor. This composite saga of Sargon, Karna, Paris, Moses, Oedipus, etc., is similar to the realization of royal lineage in delusions, in which the patient also achieves fantastic rank and honor in his make-believe world.[3] May not the interest in genealogy be attributed to this fantasy, when so many who trace their family tree seem to be descendants of exalted ancestors? It is as if one were searching for royal blood in his veins.

The fantasy of savage lineage occurs in only or favorite children of prominent or wealthy parentage. In several instances the favorite child was brought to me for irascibility and conduct anomalies. An only boy, aged 12, of unusual intelligence, associated himself with the son of his father's utility man and was the leader in petty thievery expeditions. The fantasy of having had a pirate ancestor was prominent in this boy. An only daughter, aged 28, was a constant source of trouble to her parents on account of escapades, since the age of 18, as a dancer, an actress, with two elopments and two marriages. The fantasy of having Indian blood was entertained by this patient though she was a descendant of the Mayflower Pilgrims.

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2. Our daily papers frequently serve as laboratories for the student of human conduct, as well as furnishing proof of fantasies as they exist today, which are not unlike the ancient myth fabric and dream material. The New York Times, Oct. 23, 1926, reported: "Fight in London Club Over 'Wolf Girl' Tale: The story of two little girls found living in a wolf's den in Bengal, British India, as told by the Westminster Gazette yesterday, brought the members of a well known London club to fisticuffs today after heated arguments as to whether the story is to be believed or disbelieved. . . . The Westminster Gazette story repeated that of Bishop Walsh of Bishop's College, Calcutta, who told how the Rev. Jal Singh of Midnapur, Bengal, had discovered the two girls in a distant part of his district. They were described as about 2 and 8 years of age, running on all fours, making guttural sounds and in every respect living like wolves. The supposition was that they were abandoned as babies and adopted by the she wolf. . . . Lady Dorothy Mills, noted author and traveler, said that in West Africa she had often been told by natives of small children being taken and reared by a large species of monkey, but it did not seem possible to her that anything but a very small baby could be reared by a wolf."

3. In psychotic trends the delusion of royal birth finds a counterpart in hallucinations of abuse when the patient hears voices calling him "bastard," which is an outward projection of the fantasy of illegitimacy.

Manifestations of the "Fantasy of Not Belonging to One's Family," aside from delusions, are evident in many types of neurotic actions and feelings. Most prominent is the feeling of "not belonging." Wherever such a patient goes, he feels out of place. One patient described his difficulty as follows: "When I sit in the orchestra I feel that my place is in the balcony, and when in the balcony I feel that I belong in the orchestra. As a dinner guest, no matter where I am placed, I feel that I don't belong, and in my profession (of law), whatever case I am assigned to by my senior partner finds me in the same uncertainty. In fact I feel like an outsider, and even in my home I never felt that I was one of the family." In a case of obsessional neurosis, the chief compulsive doubt concerned the patient's parentage. In her intellectual obsessions the patient generalized this first compulsion. She related that at first she would look at her mother and wonder whether she was her real parent. Later she was obsessed with the idea that she was kidnaped in childhood. When finally she became panic stricken on obsessively thinking of the origin of the world, the morbid anxiety related to her own origin.

In cases of amnesia, the fantasy is apparent. The patient loses all knowledge of his identity and behaves like a different person, calling himself by a different name and even assuming a different occupation. A patient, who was brought for treatment at New York Post-Graduate Hospital, left his father's place of business of which he was manager, and three months later was found in Baltimore working as a day laborer. Though married and the father of a child, he maintained in his amnesia that he was of a different faith, the father of several children in a city in which he had never been, and he did not recognize any of his relatives. His recovery was as sudden as the onset. An hysterical girl, who was a voluntary patient at Manhattan State Hospital, described amnesic episodes that were all related to forgetting her name and residence while going home from school. Aware of her difficulty, she made sure to go home with a classmate who lived near her, though not betraying her symptoms. In both patients, the fantasy of foster parentage [4] had been

4. An interesting example of this fantasy in its "orphan" variation is furnished again by the New York Times of Oct. 23, 1926: "Imagining Himself Orphan, Runaway Is Almost Adopted: C. C., Jr., 13 years old of ——— displayed a vivid imagination yesterday when a patrolman found him wandering aimlessly about Times Square and took him to the West Forty-Seventh Street Police Station. . . . The boy won the sympathy of all by telling them he was an orphan who had supported himself a year by selling newspapers and doing odd jobs. There was a dispute as to which of the three would adopt the attractive looking youngster. . . . At the end of the thirty minutes the boy had admitted taking $13 of his mother's money and departed to see the city."

entertained since childhood. Elsewhere,[5] I have reported a case of conversion-hysteria in which the same fantasy was manifested.

The changing of one's name, if the clue is taken from amnesic phenomena, would appear to be a manifestation of the fantasy of not belonging to one's family. In changing one's name, one estranges himself from the family with one stroke. Though the reasons advanced for the change of name are usually for business or social advantage, yet the apologetic manner with which the explanation is given and the sense of guilt connected with the change would indicate a deeper motive. The common practice among school children of adding an initial at graduation time is only a wish to change the name, and one may wonder if titles and degrees sought and bestowed may not be an unconscious catering to the fantasy of belonging to some family other than one's own. In two sets of brothers who were under analysis, the change of name was instigated in both instances by the younger brother, ostensibly for business reasons. The older brothers readily consented to the change. On further study, the unconscious motives of family conflict were discernible. In another case the patient changed his German name, of biblical origin, to "Pond," which he used outside the family circle and without their knowledge. Though he lived at home, he kept aloof from his family, was not on speaking terms with them, and regarded himself as a step-child. He rationalized his new name as being distinctly English. His dreams, however, showed that in his new name he incorporated his mother, to whom he was abnormally attached. He described many dreams about fishing in a pond in which pollutions would result. Analysis showed that "Pond" (a quiet body of water where one may find repose, etc.) referred to his mother. Several observers[6] have pointed out the unconscious determinants in changing one's name, but have stressed the factor of the ego in such change. There are undoubted cases, besides the one cited, in which the incest motive is the dominant factor. Thus one of my Jewish patients, aged 24, changed his name and married a Catholic woman, twelve years his senior. In his choice of a love object the patient showed what Abraham[7] designated as "neurotic exogamy," which is a flight from the mother or sister imago. The mother determinant was evident in spite of his flight for his wife into another creed by selecting a woman so much older than himself.

5. Lehrman, P. R.: Analysis of a Conversion Hysteria, Superimposed on an old Diffuse Central Nervous System Lesion, J. Nerv. & Ment. Dis. **54**:31 (July) 1921.

6. Abraham, Karl: Klinische Beiträge zur Psychoanalyse aus den Jahren 1907-1920, Int. Psychoan. Verlag, 1921, Leipzig, Wien, Zurich. Brill, A. A.: Fundamental Conceptions of Psychoanalysis, New York, Harcourt, Brace and Company, 1921. Oberndorf, C. P.: Reaction to Personal Names, Psychoanalyt. Rev. **5**:1 (Jan.) 1918; Internat. J. Psychoanal. **1**:3, 1920.

7. Footnote 6 (first reference).

Interestingly enough, prior to his marriage this patient was shy with girls, and the few friends he had were coreligionists. Parenthetically, it may be observed that the denial of one's nationality would belong to the same category, for only in rare instances does voluntary change of one's nationality or religion bring any advantage. One may suspect that part of the success of the Christian Science Church is the result of the opportunity it affords to belong to a family other than one's own. The epidemic of societies and secret orders also would seem to be catering to the same fantasy, for family secrecy is proverbial and the secret society fulfils this condition.

THE DEVELOPMENT AND MEANING OF THE FANTASY

In several patients, analysis disclosed that, contrary to the conscious information, the fantasy began prior to the fifth year of life and was simultaneous with the identification with the parent of the same sex. Further inquiry disclosed an incident in childhood which detrenched the patients from a formerly secure position in relation to the parents. The incident is connected with a younger brother or sister. Some favoritism toward the younger child or some deprivation suffered by the patient at the hands of the parents in favor of this younger child is remembered. The recalled incident, when studied further, appears to have assumed importance only in its function as a cover-memory. In a boy, aged 4, whom I had occasion to observe since his birth, the fantasy appeared suddenly in the following manner: While returning from a visit to his grandparents, where he was shown much attention but not quite as much as his sister, aged 5 months, who was the center of interest, he said, "Mother, I must not be left alone when you and daddy go away. A man may come and take me away and then you will have no more boy and I will be the man's boy." Further questioning as to the source of this remark was met with the statement, "I know it, no one told me about it." The fantasy of being kidnaped and adopted is condensed in this boy's remark. Children of school age not infrequently come home and relate some attempt to kidnap them, and an epidemic of kidnaping fantasies follows one actual kidnaping incident. The release of the fantasy may occur under various circumstances, and the readiness with which the fantasy appears as the result of some provocative factor would tend to prove that it is fully formed and ever present in many people unconsciously.

Since no psychic phenomenon is fortuitous, the meaning of the "Fantasy of Not Belonging to One's Family" may be arrived at from the psychoanalysis of patients. When one examines the structure of the fantasy, variously presented, there are several features constantly present. First, the patient becomes a stranger to his parents; second, there is the severance of relationship of sister and brother; and third, in the

idea of illegitimacy, there is a presumption of the impure or harlot mother. In some patients the idea of the harlot mother is projected onto a sister. Thus, one patient tells of his fantasy of finding his sister in a house of prostitution, and always suspected her when she went out socially. As the dream is the best approach to the study of the individual psyche, the citation of the following two dreams may help in the elucidation of this problem. A man, aged 24, with anxiety hysteria, dreams as follows:

> My older sister's illegitimate child dies. Someone brings the child to my other sister to have it embalmed. I kiss the dead child and fear that I am able to make it alive by such tenderness. The dead child appears to be my youngest sister.

In his associations, the patient relates that his oldest sister is about to be engaged, and he had thought about the probable sex relations with her friend. On several occasions when he entered the home unexpectedly, he found them embarrassed, and once he saw them in embrace. This sister complained several times to her mother about the way she was treated, and she said that it made her feel that she did not belong in the family. On many occasions, the patient felt that he also did not belong to the family. When he thought about the relations of his sister with her friend, he felt sexually excited. When he was younger he fantasied coitus with this sister, though at present he hates her. He recalls the birth of his youngest sister; prior to her birth he was embarrassed by his mother's condition and wished that the child would be born dead. At present he is fond of his youngest sister and is unusually attentive to her, but at times he experiences sexual impulses toward her which he dislikes. At an early age he believed that merely sitting near a woman resulted in impregnation, and for that reason avoided his older sister lest that should happen. In his fantasy of not belonging to the family, he pictured his mother as having had an affair with a lover who subsequently disappeared. The dream and his associations for it may be interpreted as follows: If he were a stranger, he could satisfy his desire for his sister without invoking the dread of incest. In the dream, his fear that he is able to bring to life his sister's illegitimate child is his wish to impregnate her. The illegitimacy of the child refers to the illegitimate relationship between himself and his sister. Again, the fear in the dream is the dread of punishment for such a relationship. The death of the child refers to his former wish for the death of his younger sister as well as castration of himself for the incest wish. That his older sister is only a surrogate mother can be inferred from his fantasy that his birth was the result of his mother's illegitimate affair. In this fantasy two conditions are fulfilled: the death of his father (the mother's lover disappears), and his mother is capable of an illegitimate relationship. The fantasy arrangement can be inverted, and then it

would be: "If father were dead, an illegitimate affair with mother could take place." The dream shows who would be responsible for bringing to life an illegitimate child, namely, the patient himself.

The second dream in three parts is that of a lawyer with anxiety-hysteria. Though I shall report the entire dream, I shall merely give that part of its analysis which relates to the fantasy.

(*a*) I am in a good sized touring car, filled with people; I am driving. Jean is in the rear seat to the right. We cross a bridge in a small town. I stop the car for a minute and don't know why. Then I drive on and notice that Jean is gone, and no one in the car seems to make anything of it. I am violently anxious about Jean, where she went to and why they let her go that way. I am very uneasy.

(*b*) A street of my childhood, it is evening, many people and dirty children, and the street is littered with dirt. I am in a touring car alone, and I park my car and enter a house.

(*c*) The setting is my own street, but not exactly like it. We live on the first floor of an apartment house, father, mother and I—but not brother. It is late evening, mother is out. Dad is in the neighborhood chatting somewhere, not a bit concerned about mother's whereabouts. I wait around for her on the street, concerned, as it is getting late. I see a woman which looks like mother from the distance. On approaching her I see a woman of mother's build, thoroughly but disorderly clad; her hat is not on straight and her face is battered, black and blue, swollen and disfigured, she looks wabbly and drunk. It is not she (mother!) and I go upstairs to wait there. The same woman then enters the apartment. She utters a sound and I recognize it is really mother! She sits in a chair gagging as if in a trance. I fall on my knees beside her, with my arms about her waist and weep hysterically. She must be put to bed and cared for as she is badly battered. Father enters and barely pays attention to the whole affair—he seems not to care. While embracing her and weeping, I awaken."

In the first and third parts of the dream, the theme is the disappearance of the beloved person. In the first part it is the disappearance of his sweetheart, and in the third part that of his mother. In the dream appears the dual concept of mother—the pure mother, the one of his conscious and ego-ideal, and the repressed concept of harlot-mother who is disorderly clad and battered and drunk. The dream is accompanied by the emotion of anxiety, and the patient awakens with that emotion; he weeps when he reflects on the content and reproaches himself. The following morning, when he related the dream to me, he sobbed hysterically, and reproached himself for having dreamed of his mother in such a light, and particularly for thinking that his younger brother was born of another father. Sobbingly he said, "And this thought strikes bitter when appearing just at this time when I see mother in this ugly light in the dream. I have thought this about five times in the last few years, for brother does not resemble either of my parents. I am certain of my parentage, for I resemble father closely." The

patient's emotional reaction to the dream showed his unconscious awareness of its meaning, though it escaped conscious recognition. In the associated fantasy about his brother, the patient remains the only legitimate child of his parents, but he betrays his doubt of the fact by stressing his certainty of it. Certainly his behavior at home was like a stranger, and his feeling of not belonging to the family (or in his profession, etc.) might have found expression in the fantasy relating to himself if it were not for the actual resemblance that he bore to his father. To circumvent this contradiction, he projected the fantasy onto his brother. Further analysis, of course, uncovered the need for the fantasy to satisfy many unconscious wishes that cannot be gone into at present, except in a fragmentary way. Evidence of his juvenile sexual craving for his mother was uncovered, such as peeping into her room while she was dressing, when he was 7 years old, and many other overtures.

It has been pointed out by Freud [8] that in the dawn of civilization the morality of man began with two taboos of totemism. One of them was the sparing of the totem animal, which was really a substitute for the father; the other was the incest prohibition. Psychoanalysis has shown further the existence of the strivings in the unconscious, which necessitated these taboos in primitive society. These strivings and taboos are contained in the well-known Oedipus complex, so evident in the delusions of psychoses and in the symptoms of the psychoneuroses. The fantasy of not belonging to the family is one of the expressions of this complex. In removing one's relationship to the family, one inverts the wish to remove the rival parent, and at the same time it clears the way for the sexual striving for the opposite parent by eliminating the dread of incest. Also the harlot-mother is accessible for these strivings whereas the pure-mother is dreaded. Thus, the fantasy in its variations and substitutes serves as a compromise between the incest striving and the incest taboo.

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8. Freud, Sigmund: Totem and Taboo, translated by A. A. Brill, London, George Rutledge & Sons, Ltd., 1919.

News and Comment

PROGRAM OF THE ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE, DEC. 28 and 29, 1927, NEW YORK

Presidential Address, Dr. Charles A. Elsberg, New York.

I. The Nature, Mechanics and General Investigation of Intracranial Pressure

1. Physiological Mechanism for the Maintenance of Intracranial Pressure. Secretion and Absorption of the Cerebrospinal Fluid. The Relation of Variations in the Circulation.
Hubert S. Howe, New York.

2. Experimental Studies of Intracranial Pressure.
Lewis H. Weed, Baltimore.

3. Intracranial Pressure Changes During Forced Drainage of the Central Nervous System.
Lawrence S. Kubie, New York.

4. The Effect on Human Cerebrospinal Fluid Pressure of Extraction and Injection of Fluid, with Observations on the Time of Normal Readjustment.
H. C. Solomon, Boston.

5. Observations of the Pial Circulation During Changes in Intracranial Pressure..
H. S. Forbes, Boston.
H. G. Wolff, Boston.

6. The Relation of the Cerebrospinal Fluid Pressure to Vascular Hydrostatic Pressure and to the Osmotic Pressure of the Blood.
Frank Fremont-Smith, Boston.
Lawrence S. Kubie, New York.

7. Experimental Changes in Intracranial Pressure and Their Relation to the Susceptibility to Convulsive Seizures in Animals.
Frank S. Pike, New York.

8. An Instrument Demonstrating the Queckenstedt Phenomena for Teaching Purposes.
Temple Fay, Philadelphia.

9. Some Experiments in Intracranial Pressure in Man During Sleep and Under Certain Other Conditions.
Lewis Stevenson, New York.
Bryant E. Christensen, New York.
S. Bernard Wortes, New York.

II. Decreased and Increased Intracranial Pressure

1. Cerebrospinal Fluid Pressure in the New-Born.

DONALD MUNRO, Boston.

2. Increased Intracranial Pressure in the Hydrocephalus of Infancy and Childhood.

KENNETH L. BLACKFAN, Boston.
BRONSON CROTHERS, Boston.

3. The Relation Between Increased Intracranial Pressure and Increased Intraspinal Pressure: the Changes in the Cerebrospinal Fluid in Increased Intracranial Pressure.

JAMES B. AYER, Boston.
JOHN S. HODGSON, Boston.

4. Convulsive Seizures Due to a General Rise of Intracranial Pressure.

WALTER M. KRAUS, New York.

5. The Mechanism and Symptoms of Increased Intracranial Pressure in Meningitis.

SIDNEY I. SCHWAB, St. Louis.

6. The Symptoms of Acute Rises in Intracranial Pressure in Cerebral Hemorrhage and Cerebral Trauma Compared with the Slower Rise of Intracranial Pressure in Tumors of the Brain.

FOSTER KENNEDY, New York.

7. The Relation Between Blood Pressure and Intracranial Pressure with Special Reference to the Changes in Intracranial Pressure After Cerebral Trauma.

CHARLES BAGLEY, JR., Baltimore.

8. The Determination of the Systolic and Diastolic Pressure in the Ophthalmic Arteries (Method of Magitot), and Its Value in the Early Recognition of Increased Intracranial Pressure.

CYRIL BARNERT, New York.

9. The Effect of Increased Intracranial Pressure on the Optic Nerves and the Eyeballs.

WALTER R. PARKER, Detroit.

10. The Fundus Changes and the Blood Pressure in the Central Artery of the Retina in Increased Intracranial Pressure — Papilledema and Optic Atrophy.

CONRAD BERENS, New York.

11. Studies of the Blind Spots and Audiometer Curves in the Presence of Intracranial Tumors.

LOYAL DAVIS, Chicago.

12. Visual Field Defects in Increased Intracranial Pressure.

GEORGE E. DE SCHWEINITZ, Philadelphia.

13. Brain Changes in Increased Intracranial Pressure.

GEORGE B. HASSIN, Chicago.

14. Changes in the Nerve Cells and the Neuroglia of the Central Nervous System in States of Increased Intracranial Pressure.

WILDER G. PENFIELD, New York.

15. The Roentgen-Ray Evidence in the Bones of the Skull of a General Rise of Intracranial Pressure (Convolutional Atrophy, Separation of Sutures, Enlargement of Diploic Channels, etc.).

H. M. IMBODEN, New York.
C. W. SCHWARTZ, New York.

III. Increase of Intracranial Pressure in Tumors and Other Expanding Lesions of the Brain

1. The Mechanism and Symptoms of Increased Intracranial Pressure Due to Tumors of the Midbrain and Tumors in the Region of the Third Ventricle.

WALTER E. DANDY, Baltimore.

2. The Mechanism and Symptoms of Increased Intracranial Pressure Due to Encapsulated and Infiltrating Tumors of the Cerebral Hemispheres.

CHARLES H. FRAZIER, Philadelphia.

3. Intracranial Pressure in Tumors and Other Lesions of the Hypophysis and Pituitary Region.

MAX M. PEET, Ann Arbor, Mich.

IV. Methods for the Reduction of Increased Intracranial Pressure

1. Repeated Removal of Fluid by Ventricular and Lumbar Puncture as a Method for the Reduction of Increased Intracranial Pressure in Expanding Lesions, in Chronic Hydrocephalus of Infancy and Childhood, in Fractures of the Skull, etc.

WILLIAM JASON MIXTER, Boston.

2. The Value of Hypertonic Solutions by Mouth, by Rectum or by Intravenous Injection for the Reduction of Increased Intracranial Pressure.

FRANCIS C. GRANT, Philadelphia.

3. The Effect of Subtemporal and Suboccipital Decompressive Operations in Irremovable Tumors of the Brain as Regards the Relief of Headache, the Preservation of Vision, the Improvement of Paralysis, etc.

GEORGE J. HEUER, Cincinnati.

4. The Recession of Choked Disks After Operations for Brain Tumor.

GILBERT HORRAX, Boston.

5. Radiotherapy in the Treatment of Increased Intracranial Pressure Associated with Tumors of the Brain.

A. U. DESJARDINS, Rochester, Minn.

Abstracts from Current Literature

THE PHYSIOLOGY OF VOMITING. V. DUMPERT, Deutsche Ztschr. f. Nervenh. **96**:8 (Feb.) 1927.

The act of vomiting is generally regarded as a defense reflex by means of which the organism may rid itself of toxic substances contained in the stomach. The vomiting after taking alkali or acids by mouth is quoted as an illustration. The vomiting in uremic and morphine poisoning is explained on a similar basis, since it is accepted that, in those conditions, the toxic poisonous substances are eliminated through the mucous membrane of the stomach, and hence are being expelled by the act of vomiting. Hatcher and Weiss, however, have called attention to the fact that the vomiting in poisoning usually takes place in too late a stage to be considered as a complete defense mechanism. Of late, many observers are inclined to consider the act of vomiting as depending on the vegetative nervous system.

There are two types of vomiting. One type takes place without nausea and the other is accompanied by nausea. The second type can best be studied in cases in which there is considerable loss of blood. The patient begins to feel nauseated, dizzy and weak; a cold sweat breaks out, a pressure is felt below the sternum, there is a ringing in the ears, darkness before the eyes, and finally vomiting occurs. According to Dumpert, the cause for the nausea and vomiting must be sought in a diminished supply of blood to the brain, and any condition tending to increase the supply of blood in the brain will also tend to diminish the feeling of nausea, such as lowering the head by placing the body in horizontal position and blood transfusion.

The lowering of the blood pressure in the brain as the causal factor in vomiting will also explain its purpose. The splanchnic area contains the largest supply of blood vessels of the body. A large part of the blood flows through that area, especially during digestion when the flow of blood is greatly increased. This, of course, brings about a diminished supply of blood to the brain. The vomiting, therefore, according to Dumpert, is a defensive reflex. By emptying the stomach, the flow of blood to the splanchnic diminishes and permits an increased flow to the brain. The so-called anemic vomiting when the stomach is empty or the early morning vomiting does not, according to Dumpert, argue against this theory, since it can be observed that other purposeful automatisms and defensive reactions of the body often are purposeless and even at times harmful.

Dumpert, therefore, sees in the act of vomiting in anemia a reaction with a specific purpose. In chlorosis, pernicious anemia, marked loss of blood in the cerebrum, or in conditions in which a large supply of blood is momentarily demanded in another organ, thus calling on the brain for its extra supply, or in all other similar conditions in which the cerebral circulation falls below normal, the stimulus for vomiting is present. Any condition bringing about an improvement in the cerebral circulation will tend to diminish or stop the vomiting; this is especially noted at times by a change in the position of the body from the vertical to the horizontal.

Dumpert holds that the vomiting in intracranial pressure is the result of anemia of the brain caused by the pressure. He denies the accepted view that vomiting of the intracranial type is usually without nausea. He has observed many patients with intracranial pressure, and he claims to have found that the

vomiting is usually preceded by nausea; only in the late stages does the nausea stop and the vomiting become more projectile, owing to the fact that the vomiting center is in a constant state of irritation as a result of the anemia of the brain.

Diminished circulation of the blood of the brain is held responsible for the nausea and vomiting in fainting, shock and collapse. As a result of a disturbance of the vasomotor center, there is a fall in the blood pressure with a corresponding temporary increase of blood in the splanchnic area. Many types of reflex vomiting belong to this group, such as the vomiting following a blow on the stomach, the vomiting following pressure on the testes or that following a tug on the mesentery. Severe pain may cause a lowering of blood pressure. Dumpert would explain the vomiting in tabetic gastric crises as being due to the same cause; the vomiting in attacks of gallbladder and renal colic and in other similar conditions is also explained as being due to an overfilling of the splanchnic vessels which brings about a cerebral anemia.

Long congestion of the brain brings about anemia of this organ, which may be followed by nausea and vomiting. This can be observed in the vomiting following severe whooping cough. Persons with arteriosclerosis become dizzy and nauseated by merely bending the head down.

The nutritional disturbance of the brain is held responsible for the nausea in intoxication. The vomiting in poisoning is looked on as a defense mechanism. The poor appetite of these patients and their objection to any kind of food indicate that digestion has stopped and food is not wanted. Alcoholic vomiting, the vomiting in gas poisoning, in narcosis, in infectious diseases and other conditions is due to the same cause.

It can be observed that the nausea present in toxic conditions can often be relieved by means which will tend to increase the circulation of the brain. Thus lowering the head after narcosis will tend to diminish the vomiting. The inhalation of oxygen will often relieve alcoholic vomiting.

There are many theories attempting to explain the nausea following stimulation of the organs of equilibrium; the most common and accepted one is that it causes a disturbance of orientation. This explanation is found in many of the textbooks. Trousseau, on the other hand, considers it primarily a vasomotor disturbance, that is, the disturbed orientation brings about a disturbance of the vasomotor system, and it is the vasomotor upset that is to be held responsible for the nausea and vomiting on stimulation of the labyrinth. Dumpert investigated this on himself. After rolling down a slope, he developed nausea and dizziness. When he stood up, the nausea and dizziness increased; when he lay down, especially so that the head was lower than the body, the nausea stopped at once, although the dizziness remained. He also found, by applying a Biers bandage around the neck, that the nausea became mild, even on standing erect. Similarly, Dumpert observed that by wearing lenses to bring about diplopia nausea and vomiting will develop and will disappear when one lies down. This is quoted as tending to prove that the nausea developed in disturbed orientation is really caused by a vasomotor disturbance.

This idea can be confirmed further by the observation that in people with diminished blood supply to the brain, even a slight stimulation of the vestibular apparatus will cause nausea. Anemic, arteriosclerotic people, with disturbance of the heart, ride badly in fast moving elevators, on the train or in street cars; they often become nauseated, and at times they vomit. Patients with a fractured skull cannot stand travel or sudden movements. Trousseau thinks there must be an association between the semicircular canals and the vasomotor center. Recently, Spiegel and Demitriades have shown experimentally that stimulating the semi-

circular canals causes a change in blood pressure which often lowered it. Stimulating the equilibratory apparatus causes a circulatory disturbance in the brain; when the stimulation is increased it causes vomiting, when the stimulation is continued for some time it results in dysfunction of the vasomotor system, and the symptoms of seasickness or Menière's disease will appear.

This conception as to the cause of seasickness makes it possible to understand the immunity that develops after being on board ship for some time and becoming more or less used to the sudden quick turns of the ship in various planes. The movements of the ship to which one is less used bring about a greater reaction and a more marked feeling of seasickness. For the same reason, nursing children will not suffer seasickness because they are accustomed to all kind of passive movements. Dumpert, therefore, considers that nausea and vomiting are due to anemia of the brain; the physiologic reason is that it gives relief to the splanchnic system, thus permitting greater circulation of blood to the brain.

BERNIS, Rochester, N. Y.

HOPES AND DISAPPOINTMENTS OF CLINICAL PSYCHIATRY. OSWALD BUMKE, Klin. Wchnschr. **5**:1905 (Oct. 8) 1926.

This article was read at the February, 1926, meeting of the Society for Psychiatric Research, which took place on about the seventieth birthday of Dr. Kraepelin, founder of the society. In 1918, Kraepelin pointed out how infantile the science of psychiatry then was, recalling, however, the rapid strides it had made in the past. When psychiatry was about to become a science, its progress was beset with difficulties. Darwinism prevailed in medicine as well as in psychiatry, and all problems were explained on a materialistic or even on a mechanical basis. As time went on, the metaphysical-mystical obliterated the materialistic, and the investigation of facts was threatened with purely literary explanations. The author is convinced, however, that "pure psychiatry" without consideration of bodily phenomena is futile, and vice versa, and, with Rudolf Steiner, believes that the two should go hand in hand. Kahlbaum vocied the thought that not only symptomatology, but cause and effect, clinical conclusions and anatomic factors belonged to the general picture of a disease; but not until Kraepelin published his textbook, in 1896, was any attention paid to it.

One of Kraepelin's chief contributions was the recognition of the difference in prognosis between manic-depressive insanity and schizophrenia, but as yet the biologic cause is unknown. Examinations of the microscopic changes in brains have revealed nothing, and, although there may be hopes of determining the biologic cause of schizophrenia, there is little hope of doing so in manic-depressive insanity. Clinical examinations and examinations of the blood, serum and glands have been of no avail, partly because of the limitations of these fields in healthy persons. These, however, are difficulties which will be conquered some day.

The simple manias, excitements, melancholias, depressions, periodic manias and melancholias and the circulatory forms were known before the time of Kraepelin. Through Kraepelin the mixed conditions and milder cases were recognized, and it was observed that in the normal periods of these persons, psychic abnormalities were present. But the more the nature of these disease entities was studied, the more their scope increased, and finally not only certain forms of psychoses of old age, but many cases of paranoia, types of neurasthenia, cases of periodic insomnia, cardiac and gastric neuroses, and other conditions, were included under this general heading of the manic-depressive. The manic-

depressive group included everything that did not terminate in deterioration. So the question naturally arose as to what was the relation or what bound together this heterogeneous disease group. In the grouping of diseases, with associated pathologic processes of the brain, it could not be overlooked that heredity apparently played a big part in some of the psychoses, but it alone did not lead to an adequate explanation.

Then there was the tendency to dominate psychiatry by psychology. Kraepelin gave an example a year ago of the experimental psychology which endeavored to count, measure or weigh bodily manifestations or results of psychic deeds by natural science. Wernicke's method, on the other hand, endeavored to unravel pathologic conditions of the brain on a basis of elementary disturbances of the brain — this method likewise was not a comprehensive but an explanatory psychology. It is clear that neither of these methods gets close to what is called the human soul, and that the necessity for intelligent understanding of the inner life of the patient becomes imperative; a comprehensive psychology necessarily arose. Such investigations are possible in patients in whom there are no anatomic conditions, and led to the idea of functional psychoses. Formerly, functional diseases were considered organic diseases with unknown anatomy, but opinions have changed, and it is now believed that functional diseases are caused by a deviation not only in the structure but also in the functions of the nerve fibers of the individual; this belief leads to infinite groups which cannot be divided, but from which certain types may be selected, even as certain temperaments are selected as types to be used as corner stones of orientation in the normal.

This does not mean, however, that recurring psychic types do not possess physical peculiarities, as pointed out by Kretschmer, for instance, that the manic-depressive type shows a pyknic habitus in 80 per cent of cases. The physical types in schizophrenia are not so constant, but through the investigations inspired by Kretschmer, other important observations may be expected. If there is a relation between psychic and physical peculiarities the question naturally arises, Why? Today one looks to chemical idiosyncrasies arising in the glands. "Endocrine anomaly" is a by-word in psychiatry as well as in medicine, but little is known of this anomaly, and until more is known, the term should be used less frequently.

Investigations into heredity, comparative observations of bodily structure and a delicate psychologic analysis are the present methods for the solving of functional disorders and allied psychopathic constitutions. In considering heredity, however, one must not lose sight of the environment, the trials and tribulations of the individual, his psychic life in all its phases and bodily injuries. A person who habitually misuses alcohol and the physician who misuses morphine are naturally abnormal; likewise, their mental attitude is specifically altered by this misuse. Also, the condition called paranoia is the answer of a psychopathic personality to certain irritations of life — it is the development of a disease which would not have occurred had the individual been dealt with less severely by the world and been spared some of the hardships of life.

The direction of research which is endeavoring to throw light on these problems is called structure analysis (Birnbaum), and it will meet many obstacles. The task is neither purely theoretical nor purely scientific. The treatment of persons who have mental disorders has by the new observation method met with fruitful collisions. What formerly seemed impossible has been made possible in some cases. It is evident that nearly every scientific research results in some practical benefit. That these benefits are slow in appearing in the field of psychiatry is easy to understand, but a glance back over the

past fifty years of psychiatric research will reveal a large amount of valuable results, and one may be thankful to Dr. Kraepelin for his inspirations and hard work along this line.

MOERSCH, Rochester, Minn.

TERTIARY SYPHILITIC MANIFESTATIONS IN GENERAL PARALYSIS, ESPECIALLY AFTER MALARIA CURE. WALTER KIRSCHENBAUM, Deutsche Ztschr. f. Nervenh. **96**:61 (Feb.) 1927.

It is uncommon to find tertiary syphilitic manifestations in metasyphilis, especially in general paralysis. When such manifestations do appear, one is inclined to question the primary diagnosis. The specific syphilitic tissue reaction is said to be the characteristic distinguishing mark between tertiary syphilis and metasyphilis. Only recently, Wilmann, in an extensive work on metasyphilis, makes the positive statement that when specific gummatous manifestations appear, the diagnosis of general paralysis must be revised.

Sträussler, however, maintains that in exceptional cases miliary gummas may be found in the general paralytic brain. In a special group of general paralytic patients who died during an acute exacerbation, A. Jakob was able to demonstrate a large number of miliary gummas and gummatous changes in the vessel walls. According to Jakob, miliary gummas and other mesodermal tissue changes in the blood vessel walls may occasionally develop in general paralysis. Those types he considers more benign in contradistinction to the more diffused unspecific inflammatory and degenerative process which he terms malignant. Spielmeyer, however, finds such differentiation unwarranted. Since many patients have shown improvement after malaria treatment, the question naturally arose: In what manner does the brain, undergoing degenerative inflammatory changes as a result of spirochetal invasion protect itself or control the process? That after malaria treatment there is no great change of the nerve tissue toward a specific syphilitic reaction which one might expect, is shown by the many cases studied histologically after malaria treatment. In neither those that showed improvement nor those that were not benefited by the treatment were any changes noticed. It is true that Sträussler and Koskinas claim to have observed a larger number of miliary gummas, indicating a change toward a benign type in harmony with Jakob's conception. But Kirschenbaum does not agree with them. Among twenty patients treated with malaria, Kirschenbaum could find only two with miliary gummas and those had not shown any improvement with malaria treatment. This would indicate that the appearance of tertiary syphilis cannot be taken as an indication of improvement. Clinically, many paralytic patients develop tertiary syphilis after treatment with malaria. Wagner von Jauregg, at a recent congress in Wiesbaden, raised the question whether the malaria treatment brings about reaction not only in the brain but also in the entire body.

Markuszewich, in 1925, reported the case of a man, aged 57, with clinical symptoms of dementia of the general paralysis type, who developed gummas of the skin over the forehead and chest two months after being cured with malaria. At the same time the patient's mental condition cleared up. F. O. Schulze, in 1925, reported the development of tertiary syphilis of the skin in three paralytic cases after treatment with malaria. The same author has a patient with a similar condition under observation, but this case has not yet been reported. Pfeiffer, in 1926, reported the case of a patient with typical general paralysis who developed a gumma of the skin one month after malaria treatment. Injections of arsphenamine cleared the skin condition. Kirschenbaum quotes a private communication from Wagner von Jauregg concerning a patient with typical general paralysis whose condition showed remission after malaria treatment. One year after the treatment, this

patient developed aphasia, agraphia and alexia, together with jacksonian attacks of the right side of the face and the arm. There were no psychic disturbances. Arsphenamine, mercury and potassium iodide brought about complete cure. Some months later, similar symptoms set in and were again cured by arsphenamine and the other drugs. Wagner von Jauregg is of the opinion that the malaria treatment brought about a more specific syphilitic reaction, which was controlled by the antisyphilitic remedies.

Kirschenbaum reports one case. A man, aged, 33, became infected in 1914. He was treated with arsphenamine and mercury. In 1918, he developed a one-sided facial paresis. In 1923, memory became poor, he lost interest in things and was obliged to give up the profession of a teacher in a high school. He developed ideas of grandeur, and he considered himself the greatest inventor; logorrhea developed, and he had no insight. On physical examination there were found: mild facial paresis; irregular pupils, with poor reaction to light and in convergence; speech not greatly affected, writing tremulous; blood Wassermann reaction +++; spinal fluid Wassermann reaction +++; lymphocytes 18/3; Nonne-Apelt test +; mastic test ++. The patient was treated with malaria. About a month later, the mental condition had improved so that he could be sent home. Three months later, he was able to resume teaching in high school. In 1925, he developed disturbance with swallowing. At that time a physical examination showed: pupils round and reacting promptly to light and in accommodation; blood Wassermann reaction ++++; spinal fluid Wassermann reaction weak with 0.5 and ++++ with 1.0 cc. Mentally, the patient was normal. An ulcer was found in the posterior wall of the epipharynx opposite the uvula, which was recognized as a gumma. It disappeared completely under treatment with potassium iodide and arsphenamine. Kirschenbaum considers this case clinically as beginning general paralysis. Malaria treatment brought a complete remission. Fifteen months later a typical gummatous growth developed in the posterior pharynx, which yielded promptly to antisyphilitic treatment.

The question must be raised: Was this a case of general paralysis? Clinically the case was carefully studied, and it would be going too far to question the diagnosis on the ground of the appearance of tertiary syphilis. It is known that in general paralysis, as a result of malaria treatment, certain physical and psychic changes may take place. This may be found in the mastic and colloidal gold curves; certain kinds of hallucinations may appear such as are more often observed in cerebral syphilis. Therefore, under malaria treatment, certain dormant characteristics of tertiary syphilis may be awakened in some cases.

BERNIS, Rochester, N. Y.

HISTOLOGIC CHANGES IN THE CENTRAL NERVOUS SYSTEM IN CATS POISONED WITH LEAD, AND THEIR RELATION TO CLINICAL PHENOMENA, PARTICULARLY CONVULSIONS. K. B. LEHMANN, H. SPATZ and K. WISBAUM-NEUBERGER, Ztschr. f. d. ges. Neurol. u. Psychiat. **103**:323 (July) 1926.

Lehmann observed that chronic lead poisoning in cats caused characteristic nervous phenomena, particularly convulsions and periods of excitement, and therefore determined to study the brains and spinal cords of these animals. Considerable experimental work had already been done in this field. Harnock, in 1878, used a solution of tri-ethyl acetate of lead in the production of lead poisoning. He found paralytic manifestations in frogs and guinea-pigs, and in dogs and cats he observed twitchings and convulsive movements. They were not accompanied by loss of consciousness and were compared by Harnock to choreiform movements in man. They could be controlled by narcosis. Stieglitz

(1892) studied guinea-pigs and porpoises in which he had produced lead poisoning. Convulsions were not observed in twelve guinea-pigs, and only twice in thirteen porpoises. The anatomic changes were many; in two animals large foci in the spinal cord were prominent, while all showed degenerative changes in the anterior horn cells of the cord, as well as in the peripheral nerves. Vulpian, Poporu and Gombault observed similar changes. It is worth noting that the earlier investigators, with their imperfect technical methods, observed changes in the ganglion cells in lead poisoning. Nissl (1892) described degenerative changes in the Nissl bodies in the ganglion cells in lead poisoning, and also severe changes in the nuclei. In 1897 he noted similar changes in the Purkinje cells of the cerebellum and in the pyramidal cells of the cortex. The latter cells showed disappearance of the Nissl bodies and increased staining of the normally unstained parts of the cell. Lugaro found similar changes in dogs who had tremors, spastic gaits and epileptic attacks as the result of lead poisoning. Spielmeyer found severe changes in the nerve cell and ameboid neuroglia in cats that died of lead poisoning. In 1909, Bonfiglio found marked thickening of the vessel walls and new formation of blood vessels in the deep layers of the cortex in dogs. Finally, Straub and Erlenmeyer (1911-1914) injected lead subcutaneously in fourteen cats, thus producing a focus of lead salts which were poorly soluble. Nervous symptoms developed in these animals after five weeks, being manifested by an uncertain gait, convulsions, and blind excitement, as well as by peripheral paralyses and difficulty in swallowing. The method of Straub and Erlenmeyer made possible the study of chronic lead poisoning in animals, by cumulative action. One of their animals examined by Aschoff showed degenerative changes in the dorsal columns and also in the eighth, ninth, tenth and twelfth nerves.

The animals in this study were poisoned by a lead compound of the following composition: ($2\,PbCO_3 + Pb(OH)_2$) with a lead content of 80 per cent. The nervous system of animals so poisoned was studied first in animals who died in convulsions, or were killed by chloroform shortly after a series of convulsions, and second, in animals who had been poisoned but who were killed after apparent recovery from the poisoning. The clinical observations show that in eleven of the twelve cats poisoned by lead, nervous symptoms appeared four weeks after the injection of lead, and among these nervous symptoms epileptic attacks were the most striking feature, occurring in ten animals. Twitchings were common, at times general and at times localized. Ataxic gait and transitory spasticity of isolated limbs also occurred. In most of the animals a change in conduct was found, such as apathy or restlessness, great fearfulness and increased excitability. In several animals, marked excitement with increased motor activity was noted. The authors point out that even in animals poisoned by similar methods the reaction to the poison is an individual one and is exhibited by different reactions in different animals.

The pathologic changes fall into three groups: (1) inflammatory, (2) fatty and (3) regressive changes in the ganglion and glia cells. Inflammatory changes were marked in only two animals. The authors believe that the inflammatory changes are an incidental symptom and that the meningitides and encephalitides which are found are not the characteristic features. The fatty changes are really part of the cellular picture. The most marked changes are found in the nerve cells, accompanied by regressive changes in the glia. The changes in the nerve cells are marked and are of the type of the severe cell change described by Nissl. The outline of the cell is vague, vacuoles fill the cells, and the cells as a whole are shrunken and much smaller than normal. This is true of the ganglion cells in both the brain and spinal cord. Alzheimer called this process a liquefaction of the nerve cells, and this process of liquefac-

tion and of regressive changes in the glia with the formation of ameboid glia cells was observed by Spielmeyer in cats poisoned by lead. These were seen also by Rosenthal, and point to the fact that the two processes go hand in hand. The foregoing changes were noted in animals that died in the late stages of lead poisoning. In cats that died of less chronic poisoning the regressive changes in the neuroglia were not found, and the changes in the nerve cells were decidedly less marked; the authors look on these changes as early stages of the more marked processes. Changes in the axis cylinder are also seen along with changes in the nerve and glia cells. These consist of mild swelling.

The changes are most marked in the spinal cord. The cells of the cortex are less markedly involved, followed by the basal ganglia and cerebellum. The medulla and cranial nerves are affected least of all. Correlation of clinical and pathologic conditions is difficult. In general, those animals which suffered most severely and over a longer period from epileptic attacks showed most marked anatomic conditions.

ALPERS, Philadelphia.

A CASE OF SUDDEN DEATH FROM CISTERN PUNCTURE. FRITZ REUTER, Wien. klin. Wchnschr. **39**:1275 (Oct. 28) 1926.

Cistern punctures are frequently employed as diagnostic and therapeutic measures, and in spite of the fact that a pointed needle is inserted very near the vital centers of the medulla oblongata, few disastrous results, especially deaths, have been observed. The author gives a report of a necropsy which he performed in such a case a few months previously.

History.—The patient was a boy, aged 14, who had been in excellent health until February, 1926, when vomiting, buzzing in the ears, double vision and dizziness occurred. The gait was like that of one who is intoxicated. Memory was unimpaired. Examination in July, 1926, revealed the following: The patient was large and strong. The right pupil was somewhat larger than the left; the eye movements were normal; sucking and chin reflexes were active. The tongue was somewhat wrinkled in the middle. Tremor of mild intention type was present in the hands. The right angle of the mouth was more poorly innervated than the left. A mild Romberg sign was present and the knee reflexes were mildly exaggerated. There was bilateral choked disk. Pressure tenderness was present in both trigeminal nerves; the corneal reflex was normal as was the sensitiveness of the occipital nerves. Stiffness of the neck, with at times clonic tremor of the neck muscles, was observed. Skull percussion revealed nothing. The finger-to-nose test was normal; the arm reflexes and abdominal reflexes were increased, and there was no latent paralysis of the legs. Buzzing was complained of in the right ear. Turning of the body three times caused swaying to the right and backward; the same was true on turning the body to the left. After the examination the pulse was 132.

On July 12, a cistern puncture was done under local anesthesia. On the first attempt, fluid came under a pressure of 290 mm. of water. Then the flow stopped. On repeated punctures, only blood appeared. The pulse was irregular, and death occurred in about thirty minutes in spite of medication.

Necropsy: In the cervical region there was a period-shaped puncture hole from which blood was flowing. The vault of the cranium was wide and oval, 17 cm. long, 14.5 cm. wide. The coronary suture was open. The sagittal suture was completely ossified and the lambdoid suture apparently was beginning to ossify with plainly visible serrations. The squamous sutures were ossified. The dura was tight and bloody. In the sinuses there was liquid, dark blood. On separation of the dura, the brain bulged out. Separation of the tentorium

revealed a crowding toward the occipital foramen of the pons, medulla oblongata and the tonsils of the cerebellum. When the brain was removed from the cranium, a flat, subarachnoidal extravasation of blood was noted at the base of the pons and in the cerebellar hemispheres at either side of the pons, especially in the region of the tonsils. Parts of the cerebellum were separated, and the fourth ventricle, corresponding to the superior vermiform process of the cerebellum was carefully opened. A mass of blood was found. When this was washed away, four small hemorrhages were revealed. At the lower left a fine puncture canal was traced from one of these hemorrhages to the medulla oblongata. The remainder of the brain was markedly edematous, the ventricles were enlarged and the ependyma was soft. No tumor mass or encephalitic focus was found. It was evident from the conditions that death was due to bleeding into the fourth ventricle following puncture of the medulla oblongata.

The history of the patient leads one to believe that there was a narrowing process in the posterior cranial fossa. Autopsy did not reveal a tumor but premature ossification of the sutures as well as chronic hydrocephalus with marked increase of pressure. This pressure, which probably had existed for some time, undoubtedly crowded the cerebellum and medulla oblongata toward the foramen magnum.

The question is, was cistern puncture justifiable? Anton does not recommend cistern punctures for tumors of the posterior cranial fossa. However, Eskuchen and others employ cistern punctures in edema of the brain following trauma and in tumors of the posterior cranial fossa. Anton would be right in his contention in this case, as the cistern was compressed. In such a patient it is easy for the needle to penetrate the medulla oblongata, and with such symptom-complexes cautious procedure is essential. In the case described it is evident that the arachnoidal block occurred at the time of operation after the fluid in the cistern was withdrawn and further insertion of the needle or aspiration should have been avoided, because the moment an arachnoidal block occurs the entire anatomic relationship is changed.

An illustration is included in this article which shows that the point of the needle was inserted a number of times. It was forced into the tissues of the medulla oblongata with subsequent disturbance of the respiratory centers; death, however, was due to hemorrhage into the fourth ventricle. This is the third death reported in the literature. The first was reported by Nonne in one of eighty-eight cases of cistern puncture. The second was reported by Eskuchen.

In conclusion, the author states that cistern punctures should be cautiously undertaken in cases in which there is a question as to the cranial capacity or volume, as occurs in premature ossification of the sutures. Central dyspnea and acceleration of the pulse may be a guiding symptom of great compression of the cistern. Critical analysis of the case reported leads the author to believe that the shortness of breath and acceleration of the pulse were the result of pressure in which the cerebellum and medulla oblongata were pressed against the foramen magnum.

MOERSCH, Rochester, Minn.

THE NEUROPSYCHIATRIC POINT OF VIEW OF THE SIGNIFICANCE OF EUGENICS FOR MARRIAGE AND PREGNANCY. S. HIRSCHFELD, Arch. f. Psychiat. u. Neurol. **77**:2 (May) 1926.

The field of eugenics as a systematic science has been made the center of a considerable discussion in recent years. From a practical point of view, present day conditions and birth control tendencies in most civilized countries, decreas-

ing the birth rate, bring up the problem of preserving the fittest by properly applied eugenics. These same conditions, however, in consideration of the fact that eugenics is dependent on studies of heredity that in man are far from conclusively established facts, would call for extreme care in application as they would necessarily make for a further decrease in the birth rate.

Our knowledge of the influence of heredity on disease and character traits in general, and mental disease in particular, consists in purely empirically obtained facts. Just what types of mental disease are transmitted hereditarily, and to what extent, is still a matter of heated discussion. None of the facts that we have are absolutely certain. Some investigators found that most psychic disturbances that are transmitted hereditarily follow the law of recessives rather than dominants, and one can expect the occurrence of hereditarily transmitted psychoses with some degree of certainty only when both parents are diseased. In the consideration of factors transmitted by the germ plasm, a distinction should be made between such as are purely hereditary and those that are due to prenatal injury. This last may even go as far back as the prezygote stage, in accordance with Weissmann's theory. Such injury could cause disease in that particular person without, however, affecting the hereditarily transmitted factors.

An important problem in this connection is that of consanguinity. Its dangers, just as those of hereditarily transmitted diseases, have been greatly exaggerated. Of recent years, some investigators have shown that unless the presence of disease in both parties has been strengthened by marriage of near relatives, or unless a continued intermarriage of close relatives has brought about a degeneration process, consanguinity will not be causative of definite inferiorities, but may even lead to a superior type of progeny. This factor has been noticed and made use of in the breeding of animals.

All things considered, one finds that only in some types of mental disturbance can we render opinion with a reasonable degree of certainty, idiocy, epilepsy and manic-depressive psychosis being fairly generally accepted as possibilities in the way of hereditary influences provided they are present in both parties. In all others, the decision will always depend on each particular case. It remains for the physician rendering the opinion to realize that he is working with probabilities rather than certainties, and that with the prevention of many poor types he may, and most probably will preclude the propagation of perfectly healthy material.

The two fields of application of eugenics in practice are marriage and pregnancy. What was previously said about the state of our knowledge of heredity in mental disease will make it clear how difficult it would be to render an opinion as to whether certain persons may or may not marry. Different states have gone as far as to request the mutual exchange of physicians' certificates between the two parties to be married. The author considers this a practical measure providing the state takes no active part in forbidding the marriage and leaves the decision to the participants. With this system, information to the public in general and to the particular persons involved, would help a great deal at any time. When the physician is asked point blank he will have to consider each case, and it will remain with the particular physician whether or not he wants to go outside the limits of the previously outlined facts.

A still more important and more difficult problem to solve is that of eugenic indication for abortions. Here not only medical, but ethical and religious factors, are involved. Most gynecologists that the author quotes are strongly

against such interference in most cases. With some neuropsychiatrists, on the other extreme, the eugenic indication is as justified as medical indications, especially because here not only the health of one person (the mother), but that of the child as well as society at large should be considered. The author takes the point of view that congenital mental defects, manic-depressive psychosis and dementia praecox could serve as justifiable indications for abortions in extramarital pregnancies.

In general, one could be guided by the following rules: the defect must be shown to be present not only in one but in both parents; it must be of the type that has been conclusively shown to be hereditary: idiocy, manic-depressive psychosis, epilepsy with psychosis, hereditary ataxia, Huntington's chorea, chronic alcoholism.

MALAMUD, Foxborough, Mass.

OTITIC MENINGITIS. W. P. EAGLETON, J. A. M. A. **87**:1544 (Nov. 6) 1926.

Using as a basis thirty-three consecutive cases of meningitis, the author presents an article on otitic meningitis. There were ten cases in which operation was performed and one in which the patient recovered spontaneously, while ten patients were not operated on because they were in a terminal stage when seen. Thirteen autopsies were performed. Eagleton emphasizes thorough removal of the source of infection, and the fact that the majority of cases with organisms in the spinal fluid are cases of labyrinthine infection. All considerations of meningitis should include that possibility following abscess of the brain, and also following septic sinus thrombophlebitis.

The problem was approached from the study of the clinical histories of the patients in the cases that came to necropsy, from an analysis of all cases in which the patients recovered from leptomeningitis with micro-organisms in the spinal fluid (reported 1921 and 1922 by Eagleton), and by a review of all the author's personal cases (over 100).

Eagleton divides septic meningitis into three stages: (1) Invasion of the subarachnoid meshes with general meningeal symptoms and pathologic spinal fluid. An operation on the mastoid is frequently followed by disappearance of meningeal symptoms because the second stage has been reached. (2) Pia-arachnoid localization. At this time examination of the spinal fluid does not reveal anything noteworthy. (3) General leptomeningitis. In the second, or even early in the third stage, evacuation through the route of infection will often control the septic process, but, of course, subarachnoid diffusion of micro-organisms is fatal.

A brief discussion of the anatomy and physiology of the pathways of the cerebrospinal fluid system with anomalies follows. Eagleton presents an operative classification of cases of meningitis in the posterior fossa and the middle fossa, with subdivisions. He discusses each division briefly and presents four cases in brief. Diagnosis of early meningitis can be made only by exacting attention to symptoms — appearance, slight restlessness, occasional vomiting, location and character of pain, pulse irregularities and occasional slowness, slight temperature deviations, alterations of the visual field, which may be transient, and external ocular paralysis. Symptoms alone may suffice to differentiate infection in the posterior fossa from infection of the middle fossa, but outside of the labyrinth and lateral sinus; only operative observation will localize the meningeal exudate.

Absence of reaction to the cold caloric test in both positions, with good hearing, occurs in terminal leptomeningitis, while absence of reaction to the same test on the side opposite the lesion in the upright but present in the

horizontal position indicates pressure; a 50 per cent reduction in turning nystagmus indicates meningeal exudate.

The author believes that there are three distinct pathologic conditions which are amenable to operation: (1) an excess of infectious fluid within the arachnoid meshes, (2) necrosis of the cerebral cortex with excessive exudate and (3) subdural meningeal exudate secondary to an abscess or suppuration of the sphenoid or accessory sinus. As to surgical treatment, there is no panacea, but the site must be determined and attacked while the infection is limited. Eagleton's principles of surgical treatment are eradication of the primary focus of infection, evacuation of the infected fluid by small dural openings with cisternal and lumbar punctures or a large dural incision in cerebral necrosis, and ligation of the common or internal carotid artery. For after-treatment, he advises repeated lumbar punctures with transfusions from an immunized donor to induce immunization of the cerebrospinal fluid system. He discusses subarachnoid irrigation and ventricular irrigation and believes the latter, especially if associated with intraventricular specific medication, may save patients in the near future. He advises from six to eight weeks of rest in bed. If there is any suggestion of increase in intracranial pressure, lumbar puncture is performed or magnesium sulphate is administered orally or rectally.

CHAMBERS, Syracuse, N. Y.

AN EXPLANATION OF THE TWO-STAGE RECOVERY OF SENSATION DURING REGENERATION OF A PERIPHERAL NERVE. JOHN S. B. STOPFORD, Brain **49**:372 (Sept.) 1926.

The author accepts Head's results of regeneration of the nerve as to cutaneous sensibility and its recovery in two stages following nerve suture, the protopathic form preceding by a considerable time the epicritic forms. Stopford divides deep sensibility also into two systems according to their manner of regeneration, the early form being characterized by appreciation of contact, of pressure and of pressure pain, the late form manifesting itself by the accurate localization of a pressure stimulus, the appreciation of posture, and the range and direction of the passive movement of a joint. In a sutured nerve the protopathic and the early form of deep sensibility return about the same time as voluntary motion commences, but the epicritic and later forms of deep sensation return much later. Their complete recovery may occur in primary nerve suture, but in the author's experience this never occurs in secondary nerve suture, the recovery being at best only partial.

Protopathic and deep sensibility, which recovers earliest, consists of cruder elements of sensation than those comprising epicritic and the system in deep sensibility which recovers later and less perfectly. An analysis of these four types of sensibility leads to their consideration in terms of Head's work on the sensory cortex which suggests that both in cutaneous and deep sensibility at the periphery, thalamic and cortical aspects of sensation must be considered. In cortical lesions and injuries of the nerve the two late or specialized forms of sensation recover late or only imperfectly. The functions of the nervous system are shown to be integrated on the principles of evolution when the systems of peripheral sensation, in the light of their recovery, are considered analogous to their representation in the cerebral hemispheres, that is, the cruder forms of sensation being represented in the thalamus, the more specialized forms in the sensory cortex. The table by the author suggests the following classification of the elements of sensations affected by division of a peripheral nerve.

I. Cutaneous Sensibility.

Thalamic (early or more complete recovery, protopathic of Head)	Discrimination of wider differences of temperature. Cutaneous pain.
Cortical (late and less perfect recovery, epicritic of Head)	Appreciation of lightest form of touch. Localization of lightest form of touch. Discrimination of finer differences of temperature. Recognition of two compass points, simultaneously applied, as two.

II. Deep Sensibility.

Thalamic (early or more complete recovery)	Appreciation of contact of pressure. Pressure pain.
Cortical (late and less perfect recovery)	Recognition of passive movement of a joint. Accurate localization of pressure.

The author rejects the theory that protopathic fibers regenerate more rapidly than epicritic. His explanation for the two stage recovery of sensation is that after nerve suture there is a distinct disturbance of the intraneural pattern; that is, the central end fibers do not all grow into the same type of end-organ but make connections with heterogeneous end-organs in their downward growth. This explains why the cruder forms of sensation return first, as a central pain fiber growing into a cold end-organ, on adequate stimulation, gives the sensation of pain; the same holds true for tactile, heat, or any protopathic end-bulbs being connected by a pain fiber. In the higher forms of sensation, as represented in the cortex, any down growth of these central fibers into heterogeneous end-organs would not produce any sensation, as if a localization fiber, previously terminated in the forearm, after regeneration grows down to a digit and reaches a tactile end-organ there. The ultimate return of the late "specialized" sensibility must be dependent to a great extent on reeducation. The return of this last form of sensation in secondary nerve suture is much more difficult owing to the greater disturbance of the intraneural pattern. In contrast to the incomplete and late return of epicritic and the late form of deep sensibility, the author cites cases of recovery of sensation following the physiologic division of a nerve, as by compression. In the latter case, following neurolysis, all forms of sensation returned at the same time, there being no two stage recovery. His explanation is that there is here no disturbance of the intraneural pattern.

Stack, Milwaukee.

The Epidural Space in its Relation to the Spinal Fluid. W. Schönfeld, Ztschr. f. d. ges. Neurol. u. Psychiat. **104**:281 (Aug.) 1926.

The epidural space has been used in the treatment of various conditions such as enuresis nocturna, certain forms of impotence and sciatica, with varying degrees of success. It has been used in spite of a lack of knowledge of its relation to the subarachnoid space, and in spite of experimental evidence to test the resorption of substances placed therein. A few experiments have been carried out. Cathelin injected dyes and after ten days found the epidural space injected, but not the subarachnoid space. Läwen and von Gaza injected methylene blue and found no injection of the medulla spinalis, medulla oblongata and the cerebellum. Moos and Warstat injected arsphenamine at the level of the iliac crests and ten minutes later recovered it at the level of the twelfth thoracic vertebra. Schönfeld knows of no other works in addition to these.

Schönfeld started out to determine the resorption of substances into the spinal fluid after injection into the subdural space. He used 147 patients and

tested the fluid and blood 264 times. He injected dyes and drugs (from 28 to 30 cc.) epidurally or parasacrally. The dyes used were aesculin, uranin, phenolsulphonephthalein; the drugs were bromides, iodides, and arsphenamine. The technic consisted in inserting a needle into the epidural space, and after varying periods of time performing lumbar puncture to determine pressure, cell count, albumin content and Wassermann and colloidal gold reactions. If the lumbar puncture was done shortly after epidural injection, the needle was left in place for some time. After-effects were seen on only a few occasions, and consisted of pain in the legs, pressure in the back, widening of the pupils and slowing of the pulse. Fluid was obtained from the epidural space on two occasions in the same case.

Of six substances introduced into the epidural space, four (aesculin, uranin, bromide, iodide) were recovered regularly in the spinal fluid, while two phenolsulphonphthalein and arsphenamine) did not appear. The passage begins immediately after the epidural injection. Bromides and iodides could be recovered fifteen hours and earlier after the epidural injection. The injected substances could not be demonstrated in the serum. They appeared immediately in the urine, as quickly in fact as on intravenous injection. This was especially true of phenolsulphonphthalein. Of the various methods of administration (mouth, parasacral, subcutaneous, intravenous) the epidural is most efficient in the transfer of substances into the spinal fluid. Thus, 100 times as much uranin appeared in the fluid in the same length of time after epidural as after intravenous injection. Bromide acts similarly, while iodide is found in the fluid only on epidural injection. It is evident that the permeability of the dura is better for some substances than others, and that it permits some substances to pass while it holds others back. This is dependent, probably, on two factors: (1) the pharmacologic nature of the injected substance; (2) the concentration. A 10 per cent solution of bromide passes over a greater quantity in the same length of time than does a 5 per cent solution. It is possible that neither phenolsulphonphthalein nor arsphenamine appeared in the fluid because their concentration was too weak. Some methods of detection of substances are more accurate than others, and it is possible mistakes were made here.

The epidural space is a good resorption medium and may be used for the introduction of drugs. Schönfeld found that bromides and iodides were quickly resorbed therefrom. Lippmann (1923) used epidural injections of sodium bromide for the lancinating pains and gastric crises of tabetics. Schönfeld cleared up the itching in two cases of eczema and one case of pruritus ani by epidural injection of sodium bromide. These substances, according to the author, should be tried in herpes and other diseases with sensory manifestations, being injected epidurally because resorption is greater from the epidural than from the intravenous method. Both iodides and bromides appear rapidly in the spinal fluid, and their injection epidurally does not cause any meningeal reaction. The method of resorption of these substances is uncertain.

ALPERS, Philadelphia.

OPTIC NYSTAGMUS AND ITS VALUE IN THE LOCALIZATION OF CEREBRAL LESIONS. JAMES CHARLES FOX and GORDON HOLMES, Brain **49**:333 (Sept.) 1926.

The object of this investigation was to determine whether in optic nystagmus, from the study of a large number of clinical cases of tumors and vascular lesions, there was a test that would prove useful in helping to localize cerebral lesions. The nystagmus was produced by having the patient follow with the eyes a revolving drum with the figures, placed 60 cm. from the patient's face. In normal persons the nystagmus is regular in rate and range and persists as

long as the drum is rotated at a uniform speed; this feature is called "well sustained." The slow component of the nystagmus is in the direction of the rotating drum, the quick component or rapid phase is that which carries the eyes to the central position or a short distance beyond; the nystagmus is always named by the quick component. The nystagmus can be produced in any person provided he can perceive the figures on the drum. This is true in cases in which blindness may be due to lesions of the optic nerves, of the chiasma, of one optic tract or of the optic radiations; homonymous hemianopia and central scotoma do not disturb optic nystagmus as shown by four illustrative cases of infrageniculate lesions. The authors insist that visual inattention in itself is not the immediate cause of loss of optic nystagmus.

In seven cases of tumors of the cerebrum, verified by necropsy, there was loss of nystagmus to the side opposite (no motion of eyeballs to side of tumor) to the lesion; the same results were obtained in four cases of tumors verified by operation. Five verified cases, four of tumors and one old gunshot wound, produced normal nystagmus. In two cases of tumor there was loss of nystagmus only for a short time. Of sixteen clinical cases of hemiplegia only about one third showed loss of nystagmus to the opposite side. Contrary to other observers, the authors cannot correlate a disturbance of optic nystagmus with any form of aphasia. In nineteen cases in which the clinical symptoms pointed definitely to cerebral tumor, only seven showed a feeble or absent response to the one side. In these cases the loss of response was always to the rotation of the drum toward the side of the cerebral lesion. The authors believe that in cases of long standing the disturbances may disappear in course of time, providing the lesion is stationary, and that the cortical activity concerned in it may be slowly readjusted as to make possible the production of a normal response. Three cases of lesions of the brain stem were presented; the results in these show that lesions that destroy voluntary lateral deviation of the eyes may abolish optic nystagmus.

In grouping the cases of cerebral lesions into those that abolish nystagmus and those that do not, the authors conclude that nystagmus to the opposite side is affected when a lesion lies in the supramarginal or angular gyrus, in the adjacent portion of the parietal and temporal lobes (the visual cortex was always intact), in the posterior end of the second frontal convolutions or along a line joining this with the angular gyrus. This last phase is illustrated by a frontal tumor and two operative incisions in the posterior ends of the second and third frontal convolutions that abolished nystagmus.

The authors are fairly well in accord with the views of Stenvers who maintains that optic nystagmus is a cerebral reflex with a centripetal center in the occipital lobe and a centrifugal center in the second frontal convolution, these two being connected by a reflex path which runs through the white matter of the hemisphere. From their own observations the authors believe the occipital lobe is concerned in it, as all lesions in this region disturbed nystagmus, but they do not feel they have definite evidence of existence of a frontal center. An interruption of the reflex path or of one of the centers is the simplest explanation of the abolishment of nystagmus to the one side of lesions correspondingly situated in the brain.

STACK, Milwaukee.

EVOLUTION OF MAN'S ERECT POSTURE. DUDLEY J. MORTON, J. Morphol. **43**:147 (Dec. 5) 1926.

Posture and locomotion are definite interactions between the organism and gravity, governed by fixed laws which pertain to the relation of the weight center to the base of support and to the action of static and kinetic forces.

The original forms of mammalian life were quadrupeds. Transition from a quadrupedal state to a saltatory state of bipedism has been established within widely separated mammalian groups and is characterized by a horizontal or inverted position of the femora whereby the right-angle position of those bones to the spinal column is retained when the body is raised to its vertical attitude. An erect cursorial type of bipedism with extended femora is seen only in the group of anthropoid apes. This type is contingent on modifications about the hip-joint so that an arboreal environment and brachiating habits are the only circumstances that would permit the necessary structural changes. Man's structure gives evidence of a long period of prehuman arboreal existence, and an interval of brachiating habits prior to his adoption of ground life is indicated by his arm-body ratio and the mobility of his shoulder joints. It seems logical to believe that human origin is correlated with the change from an arboreal to a terrestrial habitat. With this change, the human stock retained the erect posture previously acquired in arboreal life.

The semierect posture of the great apes is not an advance toward human bipedism, but it is direct evidence of the manner in which exaggerated brachiating adaptations have impaired earlier mechanical advantages for bipedism. The great apes have actually reverted to quadrupedism, and their posture is the physical result of their long arms and short legs.

Man's ancestors probably dropped to all fours frequently. They were capable of a fairly erect stance and active bipedal movements, but it was not until the independent use of the hands for other purposes than locomotion had become realized that the occasional dropping to a quadruped position was discontinued. The habitation of plains is properly associated with the early life of mankind, but that period could have occurred only after familiarity with a terrestrial environment had been attained. There must have been a transitional stage of terrestrial life within the forest between the periods of arboreal and plains-dwelling habits. The actual division of the common ancestral stem was not a sudden event, but a gradual "growing apart" of the human and of the anthropoid branches, the former becoming more and more terrestrial until eventually the split became complete. The evidence indicates that there would have been no morphologic differentiation between the members of the human stem and those of the related anthropoid groups until the former had become predominantly terrestrial in habit; because it is by modifications of the locomotor apparatus for terrestrial bipedism that the structural differences were supplied whereby the forerunners of man could have been distinguished as a separate species.

Both anatomic and biomechanic studies reveal the obstructive difficulties which inhibit the direct change of a quadruped to an erect cursorial biped; at the same time, they show that an arboreal brachiating interval had established in the ancient anthropoid stock a vertical suspended posture which automatically opened the way for a vertically supported posture on the ground. Hence, the study of animal posture corroborates the work in other fields in proving the derivation of the human stem from an ancient anthropomorphous stock, and it signifies that man has been an erect terrestrial biped from the period of his origin.

WYMAN, Boston.

ENDOCRINE-TOXIC EPILEPSY. MARK SEREJSKI, Ztschr. f. d. ges. Neurol. u. Psychiat. **105**:614 (Nov.) 1926.

Various authors speak of an endocrine epilepsy of parathyroid, ovarian, or hyperpituitary origin. The question arises whether the two are related in any way — whether the epilepsy is dependent on the endocrine disturbance. Reichardt

asserted that the endocrine system could be related to epileptic attacks. Serejski investigated the relation of the thyroid gland to epilepsy, studying various thyroid disorders.

Hypothyroid epilepsy is not any more common than the combination of hypothyroidism with other diseases. According to Marchand, epilepsy occurs in myxedematous idiots less often than in other forms of idiocy. Paris asserts that patients with goiter develop fewer epileptic attacks and never develop status epilepticus. If epileptic patients develop a goiter the attacks lessen in intensity and often disappear completely. This was observed in a case by Kowalewsky. Hypothyroidism seems to be a safeguard against epilepsy therefore. On the other hand, others have reported marked epilepsy with hypothyroidism. Hirsch, Guitto and others report epileptic attacks in myxedematous cases. Epileptic attacks often occur after thyroidectomy. Bastin, Bolten and other assert that hypothyroidism may call forth a latent epilepsy. Parhon and Goldstein connect hypothyroidism with epilepsy by the decrease in the calcium content which is found in the latter condition. Histologically, there is a demonstrable connection between the thyroid and epilepsy because in the majority of cases of epilepsy there is decrease in the weight of the thyroid gland. These histologic changes are variable. French authors report a sclerosis, while German authors do not find any changes. Thyroid therapy in epilepsy is uncertain; at times good results occur while at others the feeding of thyroid extract has been known to bring on epileptic attacks.

Epilepsy has been connected with dysfunction as well as loss of function of the thyroid gland. Buscaino attributed epileptic attacks to an anaphylactic phenomenon due to albuminous products of thyroid origin, caused by thyroid dysfunction. He found these albuminous products in 71 per cent of the thyroid glands of epileptic patients. Parhon also has found it in ten of fifteen cases of epilepsy.

The combination of epilepsy and hyperthyroidism is rarely seen. Serejski reports four cases of epilepsy, however, in which hyperthyroidism was present. He considers his patients as having a hereditary epileptic background and calls them "epileptoid psychopaths." He thinks there was a capability for epilepsy in these patients which was present from the beginning, and subscribes to the "epileptischen Reaktions-fähigkeit" of Redlich and the "konvulsiven Reaktionsfähigkeit" of Frisch. The thyrotoxicosis in these four cases was merely the irritative factor or stimulative factor necessary to cause an epilepsy in an organism which had the power to react by convulsions, and only needed the incentive to react in this way.

ALPERS, Philadelphia.

SPONTANEOUS SUBARACHNOID HEMORRHAGE WITH RECOVERY. REMARKS ON THE AETIOLOGY OF SUCH CASES IN THE ABSENCE OF ANY OBVIOUS RENAL OF VASCULAR DISEASE AND WITHOUT ANY KNOWN INFECTION OR GENERAL TENDENCY TO HEMORRHAGES OF ANY KIND. F. PARKES WEBER and O. BODE, J. Neurol. & Psychopath. **8**:39 (July) 1926.

In some fatal cases the spontaneous subarachnoid hemorrhage may resemble those of general increased intracranial pressure from hemorrhage into the ventricles. From the rigidity of the neck, Kernig's sign, and the usual presence of pyrexia, a diagnosis of meningitis has frequently been made. The occurrence of lethargy and somnolence, as in the present case, has resulted in various cases in a diagnosis of epidemic encephalitis. In other cases this form of hemorrhage has been associated with hemorrhages into the retina.

The case here reported is that of a woman, aged 54, who since 16 years of age had suffered from migraine-like attacks (vomiting and pain on the left

side of the head) every six weeks. She suddenly developed severe pain in the head, fell into a condition of somnolence and was sent to the hospital with a diagnosis of epidemic encephalitis. She could be aroused and then complained of tiredness and sleepiness. The left pupil reacted more slowly than the right, but otherwise the neurologic and general examinations gave entirely normal results. The eyegrounds were normal; the blood pressure was 180 systolic, 120 diastolic. Lumbar puncture on two occasions revealed a fluid uniformly mixed with blood; after centrifuging, the supernatant fluid was yellow and gave positive reactions for hemoglobin and bilirubin. The patient gradually recovered without any definite localizing signs. During the course of the illness, moderate pyrexia, as noted in other cases, was present. The Wassermann reaction with both blood and spinal fluid was negative; the blood count was normal, the blood coagulability normal. There was no tuberculosis, injury, infection or any renal or cardiac condition present to account for the hemorrhage.

After separation of the red corpuscles, a positive Hijams van den Bergh indirect reaction for bilirubin, when checked against the blood plasma, indicates that the blood was present some time before the puncture, the hemoglobin being transformed into blood bilirubin.

In the discussion of the causes of spontaneous subarachnoid hemorrhage, rupture of a small aneurysm, due to some developmental defect in the vessel wall, is one of the most likely causes. Rupture of a defective artery without a preformed aneurysm must also be considered. A number of cases have been reported in which "rents" in the internal elastic lamina were found on examination of otherwise normal vessels. Vasomotor disturbances may be a factor, especially when there is such a relationship between migraine, present in this case, and resulting intrameningeal and intra-ocular hemorrhage such as has been known to occur.

STACK, Milwaukee.

THE NATURE OF SO-CALLED PATHOLOGIC REFLEXES. I. N. FILIMONOFF, Ztschr f. d. ges. Neurol. u. Psychiat. **103**:416 (July) 1926.

An anatomic interpretation of the Babinski phenomenon, as well as other pathologic reflexes, is not sufficient to explain these interesting signs. The anatomic conception is not only the oldest, but also the most widely accepted. As Babinski himself pointed out, the occurrence of the reflex which bears his name is indicative of a lesion of the pyramidal tract. This is not generally true, however. There are cases of transverse lesions of the spinal cord with maximal degeneration of the pyramidal system in which this sign does not occur. Guillain and Barré, in seventeen cases of complete transverse lesion of the spinal cord, found plantar flexion in sixteen cases, and actually concluded that this reaction was pathognomonic of a complete transverse lesion, while the Babinski phenomenon occurs only in partial degeneration of the pyramidal tract in the spinal cord. In amyotrophic lateral sclerosis, moreover, the Babinski sign is often either slight or absent. It is not sufficient, therefore, to explain the Babinski phenomenon on a pure lesion of the pyramidal tract. There is some other element. Rudolf has pointed out that in primates the plantar reflex is always with extension, while Minkowski has found plantar extension and flexion in macacus monkeys. Marie and his school look on the Babinski sign as an integral part of a shortening reflex, and place it in the group of metameric automatisms. O. Foerster, in 1906, put forth a similar view. Others, however, think that the Babinski phenomenon is not a shortening but a lengthening reflex. Others, such as Armenise, connect it with the extensor apparatus and extensor tonus. Astwazaturow looks on the Babinski sign as a reappearance of the grasp reflex in which the big toe extends and the other toes flex. Foix and Alajouanine

consider the Babinski sign due to a lesion of the pyramidal tract and the defense reflexes to an extrapyramidal lesion.

Filimonoff divides the pathologic reflexes into those causing extension of the big toe — Babinski, Oppenheim, Gordon, Schäfer, Redlich, Thommer — and those causing the flexion — Rossolimo, Mendel-Bechterew, Jukowski, Bechterew. He considers the problem a clinicophysiologic one, and attacks it from the angle of metameric automatisms. He says that at times a plantar and dorsal reflex of the types of Rossolimo and Babinski may be seen more or less isolated. In some cases flexion is more pronounced, in others extension. In these reflexes are found examples of reciprocal antagonistic reactions, as seen in shortening and lengthening reflexes. "Dorsal reflex of the toe of the type of Babinski must be looked on as a component of the general shortening reaction (flexion reflex)." The basis of this is seen in: the nociceptive nature of the stimuli, their reflexogenous zones, the synchronicity with the general flexion reflex, the relation to the neck phenomena of Magnus and Kleijn, and their independence of spasticity and increased tendon reflexes. Plantar flexion of the big toes of the type of Rossolimo are looked on as components of the lengthening reaction (extensor thrust of Sherrington).

ALPERS, Philadelphia.

CONSTITUTIONAL PSYCHOLOGICAL FACTORS IN PSYCHOSES. HELGE LUNDHOLM, J. Nerv. & Ment. Dis. **64**:125 (Aug.) 1926.

McDougall regards the manic-depressive disorder as resulting from disturbance of the normal balance of self-assertion and self-submission. The author, starting from McDougall's hypothesis, builds one of his own on classification of altrocentric and egocentric traits of personality. The altrocentric traits are extrospective, extro-active and sympathetic; the egocentric traits are introspective, seclusive and egotistic. A well adjusted conduct is determined by a balance of all six traits, and combinations of these types can occur. The altrocentric traits combine easily with each other on the one hand, and the egocentric with each other, on the other hand. This tendency leads to the distinction between extrovert and introvert. Introversion and egocentricity in the prepsychotic personality is a bias in favor of dementia praecox; extroversion and altrocentricity favor manic-depressive psychoses. These altrocentric and egocentric tendencies are present at the birth of the individual. Many extro-active and extrospective persons are not sympathetic, for society interests them only as a means of self-display and self-assertion. Such a person is fundamentally egocentric. Thus, too, while the self-assertive tendency might be furthered by both altrocentric and extrovert tendencies, the self-submissive is entirely excluded by the egocentric tendency. Both the depressed and the manic patient lack sympathy for others; in the former, there is disability of self-forgetfulness, and faulty valuation of things resulting from overconsideration of the self, to the extent that he has no room for deep feelings for others. The agitated depression asserts himself in the direction of extreme self-humiliation. The author regards the patient of manic-depressive type as being furnished with both altrocentric and egocentric tendencies, the latter being stronger than the former. In dementia praecox, however, the extrovert tendency is much stronger in relation to the altrocentric tendency than in the manic-depressive type. Hence, the author concludes that true sympathy is the only real source of happiness and never leads to insanity, and that more fundamental than McDougall's instincts of self-assertion and self-submission are these altrocentric and extrovert tendencies which may make use of either of those instincts.

HART, Greenwich, Conn.

SYMPTOMATOLOGY AND OPERATIVE TREATMENT OF SPINA BIFIDA OCCULTA. POUSSEP, Folia neurop. Eston. **5**:81, 1926.

Spina bifida occulta is a developmental anomaly of the vertebral column in which the laminae, less frequently the bodies of the vertebrae, present a fissure through which the contents of the vertebral canal do not herniate. Infrequently there is a tumor over the site of the fissure. Occasionally the tumor may lie within the vertebral canal and produce compression of the spinal cord. Spina bifida occulta may not be accompanied by cord or root symptoms. The diagnosis before the discovery of the roentgen ray was accompanied by considerable difficulty, but was made on certain signs, particularly hypertrichosis. The hair over the opening might reach a length of 12 inches (30.48 cm.), and resemble a tail, or a mane if the condition were present in the neck. The hypertrichosis is probably due to hyperplasia of the skin as suggested by Virchow. Nervous symptoms, such as pes equinus or incontinence of urine or feces, establish the diagnosis. Sometimes one finds a nevus and almost always a scarring or dimpling over the site.

Recklinghausen believed that spina bifida occurs as a result of rupture of a myelomeningocele with later growth of hair and scar formation. The most frequent location is the lumbosacral region. The author reports two cases with typical symptoms, in which, in addition to incontinence, there was radicular hyperesthesia. It seemed that the incontinence was due to hyperesthesia of the vesical mucosa rather than to paralysis of the bladder. At operation linear fusion of the dura with the remains of the laminae was found, so it was obvious that these strands in movements of the vertebral canal must drag or compress the roots, stimulating the roots insufficiently to give rise to pain, but enough to cause hyperesthesia of the skin and of the vesical and rectal mucosae. The operative treatment consisted in section of the strands and closure of the fissure. This closure should be performed by implanting a spinous process in the fissure so that the dura and skin or muscles should not become fused again. After all, the symptom-complex of the disease is not due to the fissure, but to the adhesions. These adhesions are probably the result of obliteration of the spina bifida cystica formerly present. The author advises that, in cases of nocturnal enuresis and urinary incontinence with no adequate explanation, a roentgenogram should be made and if spina bifida occulta is disclosed, operation should be performed.

In the third case the general complaint was severe lumbago. A similar picture was found. In this case, in addition to freeing the adhesions, Poussep practice the Albee operation of immobilizing the spinal column by bone graft. This procedure in this case was followed by relief from pain.

FREEMAN, Washington, D. C.

THE PREVENTION OF INSANITY—A PRELIMINARY SURVEY OF THE PROBLEM. GEORGE M. ROBERTSON, J. Ment. Sc. **72**:299 (Oct.) 1926.

This seventh Maudsley lecture does New York the compliment of basing its statistics on the Twenty-First Annual Report of the Commission in Lunacy of that State. The writer restates in a clear way Dr. Pollock's statistics concerning incidence as affected by sex, civil condition, age and different kinds of mental breakdowns. He mentions the observations of Dr. Carswell in selecting five wards in the city of Glasgow with a population of about 200,000 and a low death rate and another five wards with the same population and a high death rate. He found that in the so-called healthy wards there were 165 patients with first attacks of psychoses under the age of 45, and in the unhealthy group,

186 patients. However, the incidence of psychoses in people over 45 was 65 in the healthy and 149 in the unhealthy wards. His conclusion is that improved social conditions reduce the number of senile psychoses. His work apparently leaves out the consideration that as good social conditions lengthen the average life they bring about an increase in senile mental disorders.

Dr. Robertson then turns to means of prevention. Eugenics he passes by with the remark that it is "a social duty on the part of those inheriting a neuropathic strain to avoid marriage into stocks of similar weakness." He states the importance of mental hygiene in children, briefly but clearly. His consideration of the influence of alcohol is practically the statistics of the Royal Hospital at Morningside from 1907 to 1920. These statistics do not convince one of any marked trend as the percentage of admissions of men due to alcoholic excesses was 13.6 in 1907, and 13.3 in 1920. The percentage of admissions of women decreased from 9.2 to 1 in the same period and the average for women for the seven years previous to 1913 was 9.6 as compared to 2.6 in the seven years following. Apparently, 1911 was a bad year for drinkers in Edinburgh, as the percentage of admissions of men was 28.9 and of women, 9.7.

The author considers at some length the effect of education and arsphenamine on general paralysis. The annual number of deaths from this disease in England and Wales continued to be steady from 1907 to 1918, but in 1919 there was a drop of 26 per cent in the number of deaths, and this low level was held through 1924. The author ascribes this drop to the use of arsphenamine in 1910.

Scotland, with a population of 4,750,000, from 1910 to 1914, had a total registered insane group of 18,537 and a group of first admissions averaging 2,828. For 1915 to 1919 the figures were 4,850,000, 18,132 and 2,762. For 1920 to 1924, the same figures were 4,870,000, 18,044 and 2,831. Such regularity is astonishing.

BOND, Philadelphia.

A HEMORRHAGIC CYST OF THE THIRD VENTRICLE, CAUSING A PECULIAR NEUROPSYCHIATRIC SYNDROME. L. MARCHAND and M. CHATAGANON, Ann. d'anat. path. **4**:314, 1927.

A woman, aged 57, presented a psychasthenic state, characterized by depression, anxiety, irritability and various phobias. Eight years previously she had been in the hospital for four or five months with meningeal hemorrhage or hemorrhagic meningitis, which came on with a stroke during work and was characterized by severe headache and vertigo. Cardiorenal disease was established. In 1926, an examination showed marked obesity and dementia. There was a peculiar state of somnolence and mental retardation. The lower limbs were in extension with slight hypertonia, the tendon reflexes being lively without clonus, although a Babinski sign was obtained on each side. There was hyperesthesia to touch and hypesthesia to heat and cold, with marked disturbance of the deep sensibility. In attempting to stand, the patient fell over backward, and there was reduction and slowness in voluntary movements of the upper limbs without marked deviation of the tendon reflexes or of sensation. The spinal fluid was essentially normal.

During the days following admission, the symptoms all became accentuated, and on May 22 Cheyne-Stokes respiration developed. There was a period of improvement, however, lasting a week, with disappearance of the somnolence, but there was rapid psychic fatigability. Peripheral facial paralysis appeared one day and disappeared the next. Disorders of the sphincters and weakness of the limbs remained. The terminal stage began with fever, vomiting and coma.

At necropsy there was marked atheroma of the basilar arteries. On separation of the hemispheres a hard black tumor, the size of a large almond, was found occupying the third ventricle and pressing its walls. On microscopic examination this tumor was found to be an encysted hemorrhage, showing no connection with the walls of the ventricle. There was considerable fibrous tissue reaction of the periphery with numerous calcified areas.

This is an unusual case, showing a fairly pure syndrome of the third ventricle although there was no polyuria.

FREEMAN, Washington, D. C.

A STUDY OF THE NEST-BUILDING ACTIVITY OF THE ALBINO RAT. ELAINE FLITNER KINDER, J. Exper. Zool. **47**:117 (April 5) 1927.

The nest-building activity of the albino rat is a specific and variable form of behavior, contributing to the thermal regulation of the organism, initiated by the peripheral sensation of cold and inhibited by heat. It is present at the twentieth day of age, is relatively independent of learning, appears in both sexes, and is maintained at a fairly constant level throughout the life of the animal. Within the limits of normal temperature, higher temperatures are accompanied by a decrease in nest-building and lower temperatures by an increase. An increase in relative humidity at low temperatures tends to increase nest-building. At temperatures above 80 F., the nest-building activity ceases for all animals except mothers suckling young. At continued temperatures below 56 F., the nest-building activity of young animals ceases as the sluggishness from exposure to cold increases. The nest-building of adult animals continues through a drop in temperature to 40 F. Nests constructed during low temperatures are compact, while those built during high temperatures are loose and scattered.

The nest-building of the adult female rat shows cyclic variations synchronous with the estrus cycle, the maximum of nest-building occurring during the diestrus interval and the minimum at the time of estrus. The nest-building of the female shows a great increase at the time of parturition and during lactation. An increase in nest-building is accompanied by an increase in food intake, and a decrease in nest-building by a decrease in food intake. The thermoregulative function of the nest is further shown by: the increased nest-building of prepubescence, lactation and starvation; the correspondence between nest-building and food intake, and by the fact that nests are invariably built when the circulation of air is at a minimum, i. e., in a corner or against the wall of the cage. As a thermoregulative activity, nest-building suggests a biologic basis for the shelter provided by the higher animals for whom the more primitive means of heat regulation are inadequate.

WYMAN, Boston.

SYPHILIS OF THE CENTRAL NERVOUS SYSTEM. JOSEPH SMITH, Am. J. Syph. **10**: 545, 1926.

Two types of reaction to syphilis of the nervous system are described. First, the chronic inflammatory process due to proliferation of the mesoblastic elements, and second, the widespread degenerative change in the parenchymatous structures. The first group includes syphilis of the blood vessels, meningitic reactions and gummas. The second is characterized by the shrinkage and pigment degeneration of motor cells, lymphocytic infiltration of the adventitia of blood vessels and of the pia, and proliferation of neuroglia cells. The nervous system may become involved at an early stage. The author has seen symptoms of syphilitic meningitis

develop four or five months after the primary infection. The lymphocytosis which sometimes appears with the eruption is not a sure sign of involvement of the nervous system, and may occur with nonspecific febrile reactions. The conditions which favor involvement of the nervous system in one case and not in another remain undetermined, although early systematic treatment seems to afford the best chance of escape from general paralysis or tabes. The tendency to variability of symptoms is pathognomonic of the disease. Vascular changes account for the thrombotic processes seen in young people without heart disease. In syphilitic basal meningitis there is usually involvement of the cranial nerve or hydrocephalus, whereas gummas may give rise to compression or motor irritation. Sudden changes may be due to the tendency for gummas to disintegrate in older foci and to attack new regions. General paralysis and tabes, on the other hand, do not show abrupt changes. The diagnosis may usually be made on the age of the patient, a history of specific infection, cranial nerve palsies, paresis or paralysis of an extremity, the condition of the deep reflexes and of the pupils, sensory disturbances, and finally on the spinal fluid examination. In epidemic encephalitis there is usually a history of preceding sore throat or grip, and it shows more abrupt changes in the physical signs and a more profound somnolence. In multiple sclerosis, nystagmus and disease of the optic nerves are more common. Illustrative cases of parenchymatous and vascular neurosyphilis are quoted.

JENKINS, Philadelphia.

FOX-FORDYCE DISEASE ASSOCIATED WITH HYPERTHYROIDISM. E. W. NETHERTON, Arch. Dermat. & Syph. **13**:794 (June) 1926.

Since the original description of this rare condition by Fox and Fordyce, in 1902, about thirty cases have been reported. Most of these cases have occurred in neurotic women, but in most cases there were no symptoms which adequately explained the neurotic condition.

The author reports a case which seems to have been definitely associated with hyperthroidism. A woman, single, aged 21, was first seen in December, 1923. She had a papular eruption in the right axilla which had been accompanied but not preceded by intense itching. In March, 1924, the left axilla was similarly affected; a short time later the pubic hair was involved, and in December, 1924, the breasts showed lesions. The itching was intense, paroxysmal, and worse at night; the hair of the affected regions almost entirely disappeared. The patient was slightly nervous; physical examination gave essentially negative results. The urine, blood counts and blood chemistry were normal; the Wassermann reaction was negative. Biopsy examination showed the pathologic process characteristic of this disease. Roentgen-ray exposures, sedatives and antipruritics proved of no benefit in treatment; nervousness and irritability increased, a tremor developed, the pulse rate increased to 118, and the basal metabolism in March, 1925, was plus 95. Thyroidectomy was done in May, 1925. Four months later the metabolic rate was plus 25; the pulse rate, 82, and the itching was less severe; nervousness was lost; the patient gained in weight and the size of the lesions decreased.

The literature is reviewed, and the obscurity of the etiology and the failure of the usual treatment are commented on. The author concludes that in this case thyroid toxicosis was probably the basic etiologic factor and suggests that thyroid dysfunction or hyperfunction may be a definite factor in the production of this condition.

KUBITSCHEK, Philadelphia.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, April 21, 1927

JOHN FAVILL, M.D., *President, in the Chair*

SOME RESULTS OF ENDOCRINE THERAPY IN BEHAVIOR DISORDERS OF CHILDREN; A PRELIMINARY REPORT. DR. SARA GEIGER (by invitation).

Twenty children showing evidences of glandular imbalance, who were referred to the Institute for Juvenile Research on account of behavior disturbances involving poor judgment, restlessness, lack of concentration and difficulties arising from mental deficiency or a feeling of inferiority were treated with gland extracts. These children have been studied, usually at weekly intervals, over periods ranging from six to thirty months, to determine the effect of the treatment on mentality, physique and behavior.

Pituitary substance given by mouth produced no change either in the physical condition or in behavior. An attempt was not made to elevate a low metabolic rate above a high normal plus rating; with the dose of thyroid sufficient to do this, loss of body weight did not occur; however, the emotional reactions became more stable. Pituitary extract given hypodermically in increasing doses produced no change in physique; however, the children with mental defect became less restless and were not so definitely alien in a normal social group. A carefully selected diet, low in carbohydrates and fats, alone or in any combination with the aforementioned substances, produced a diminution in weight, which occurred more promptly in combination with thyroid substance.

Pituitary extract administered hypodermically and thyroid substance administered orally, singly or combined, produced definite changes in behavior consisting of less sullenness, less restlessness, more stable emotions, and better concentration, leading to improved adjustments in home, school and play.

The results secured indicate that there are advantages in endocrine therapy. Further data, including laboratory observations, roentgenographic study of bone growth, visual fields, growth curves, statistical data and the relation of sex problems to endocrine pathology are in course of preparation.

DISCUSSION

DR. LEWIS J. POLLOCK: This paper should not pass without some comment, because it exemplifies an exceedingly wholesome type of report. For many years we have been concerned with the various attempts to study behavior difficulties in children, but few reports have been forthcoming that gave us any opinion as to the results of treatment. I wish to express my gratification that here is an attempt, in a small way, to tell what has been accomplished.

DR. PETER BASSOE: I think that this report is one of the most practical and useful that has come to us from the Institute for Juvenile Research. I hope it is only preliminary and that more will follow. The difficulties of studying endocrine treatment in children are that we have had so many scattered reports, while few institutions have carried on consecutive work on cases over long periods. It seems to me that this Institute is particularly adapted to carry on such work over long periods of time and thus produce statistics that will be of value. Work of this kind is now being carried on perhaps most extensively at Lisser's Clinic in San Francisco. Engelbach has done a great deal of work, and one of his side lines I think is most valuable; that is, the study of changes in ossification in endocrine cases. I wonder whether Dr. Geiger has done anything with that phase of it. It is well worth while in

institutions in which there are facilities for roentgen-ray work to accumulate data regarding signs of premature or delayed ossification; it is helpful in distinguishing between different types of endocrine disorder. If this work can be continued for years and the patients followed to adult life, valuable results will be obtained.

I heard Dr. Geiger say that some of the children were receiving 18 grains (1.16 Gm.) of pituitary extract by mouth and apparently not receiving benefit, and that when the extract was administered hypodermically improvement followed. Carlson says that the only gland product that is active when given by mouth is the thyroid; all others are inert when given in that manner.

Dr. George W. Hall: This subject is of importance to the layman as well as to the physician. I have had occasion to observe some cases along the lines mentioned; one girl has been under my care for three years. She was about 50 pounds (22.7 Kg.) overweight and now is about 25 (11.3 Kg.). When I first saw her she was so nervous that the mother could not live with her. The girl is of high intelligence and always secured high grades in her school work. I saw her about two weeks ago, and she is a changed person. She has become quieter and is much more reasonable in her requests at home; she has done gratifying work in school in the past year. I have given her the whole pituitary gland, but never any pituitary extract hypodermically.

Have the effects of endocrine disturbances been observed at the Institute in postencephalitic cases? A young man now under my care had encephalitis and then peculiar epileptiform attacks; this stage was followed by marked increase in weight, which has since been lost. Now he has marked hyperthyroidism, his basal metabolic rate being +66.

Dr. Meyer Solomon: I should like to ask about the metabolic variation in children. One child now under observation was reported to have a metabolic rate of +42. The test was repeated yesterday and was +21. An article in the literature gives the normal variation as from +20 to −20. What has been observed at the Institute, and is this the normal range for the average child?

Dr. Geiger: We have had no way of taking extensive roentgenograms and we took them only in cases in which there was marked pituitary disturbance. We hope to go on with this work. We have not obtained any favorable results from the administration of pituitary substance by mouth. I hesitated to report this because Lisser, Engelbach and others report decrease in weight when pituitary substance is given by mouth. We have been watching the postencephalitic cases, but so far we have not seen any endocrine changes.

Basal metabolic rates have been estimated only in children with enlarged thyroid glands or in those who had shown great glandular disturbance. In those cases we have not been governed by the metabolic rate unless there were other conditions that would indicate lowered thyroid activity. We have used a range of from +15 to −15 as limits for the normal metabolic rate.

Incidence of Syphilis Among Criminals. Dr. Walter B. Martin (by invitation).

Wassermann tests on 1,335 prisoners at the Illinois State Penitentiary, Joliet, revealed 13.5 per cent positive reactions in white inmates and 30 per cent in negroes, with an average of 18.2 per cent. Negroes make up only 25 per cent of the population at the prison and 28.3 per cent of the persons studied; they provide, however, 46.5 per cent of the positive reactions.

Interrogation does not reveal accurately the prevalence of syphilis. Only 34.6 per cent of the white prisoners and 42.5 per cent of the negroes who were found to have syphilis acknowledged having it when admitted. Many continued to say that they did not have syphilis even when they had positive reactions to the Wassermann test.

Taken as a group, there were no more instances of criminal recidivism among syphilitic than among nonsyphilitic men. When separated according to

color, the percentage of recidivism was somewhat higher among white men with syphilis than among those with negative reactions, but was less than in the general white population of the prison. The reverse was true in negroes. This appears to be due to an accidental factor in the ratio of the different types of crime represented in the cases studied.

Men convicted of crimes of fraud showed the highest ratio of syphilis, 24.5 per cent; those convicted of murder were second with 24.2 per cent, and the sex group was lowest with 12.8 per cent. In all crimes the ratio of syphilis among negroes was higher than among white men. In cases of crimes of murder and robbery, the ratio was three times as high for the negroes.

Men, aged 31 or more, appear in a higher percentage in the syphilitic than in the nonsyphilitic group. The reverse was true for men, aged 25 and less. The tendency toward the upper ranges of age was more marked among syphilitic white men than among syphilitic negroes. The percentage of syphilitic persons who entered prison after the age of 30 was 48.7 for white men and 38.6 for negroes.

The age at infection was given as below 21 by 60 per cent of negroes and by 25 per cent of white men; the disease was acquired before 25 by 65.3 per cent of white men and by 86.8 per cent of negroes.

In both the white and colored groups, a higher percentage of syphilitic men than of nonsyphilitic men was married.

Divorce was more frequent among the syphilitic group and separation more frequent among the nonsyphilitic. Divorce was preferred by the white men and simple separation by the colored in both syphilitic and nonsyphilitic groups.

In the syphilitic group of men, 40.5 per cent were mentally defective by the army alpha test; in the nonsyphilitic group, 23.3 per cent. Of the syphilitic men, 7.2 fell in the group of superior intelligence; of the nonsyphilitic, 11.3 per cent.

Approximately 50 per cent of the syphilitic men had not been treated prior to admission to prison. Treatment was persevered in much better by white than by colored men; the percentages of failure to obtain treatment, however, was about the same in the two races.

Approximately 50 per cent were infected within the five years before admission to prison, and 19.4 per cent within one year. The infection had existed for sixteen or more years in 8.8 per cent, the ratio of white to colored men in this respect being approximately equal.

In the group of white recidivists, 39.3 per cent dated the infection back more than ten years, whereas this was true of only 17.1 per cent of first offenders. For the negroes, these figures were 16.7 and 24.1, respectively.

Syphilis is a symptom of the social behavior of many criminals leading up to, but probably not causing, criminal acts that warrant imprisonment. The high incidence of old infections in white recidivists and the prevalence of syphilis in the groups of murderers and robbers deserve further investigation.

DISCUSSION

Dr. Herman Adler: This work is particularly interesting because it covers some of the observations previously made in the penitentiaries. We find as a result of Dr. Martin's work that the word of a prisoner is as unreliable in this work as in many others, and that the records were relied on more than they should have been. The laboratory work was checked carefully by having specimens sent to other laboratories from time to time, and the work of the state laboratory is to be commended for its accuracy as proved by other laboratories. I think the myth of syphilis in connection with crime has been shattered, though I was recently asked if I thought syphilis caused two thirds of all crime and alcohol the other one third.

Dr. Peter Bassoe: How many of these prisoners actually had neurosyphilis? Did general paralysis or syphilis of the nerve explain their conduct in any of them?

DR. WALTER B. MARTIN: I purposely avoided mentioning that, although I have some information. Prisoners sometimes oppose the taking of spinal fluid tests. In this group, I have detected twenty-eight cases, or about 10 per cent, with associated signs of neurosyphilis. The majority of these break down in the institution and some have been amenable to tests. I think because of the youth of our patients, the average age being 26, there are not many who have been infected sufficiently long to show general paralysis.

ENURESIS IN ADOLESCENT BOYS. DR. PAUL L. SCHROEDER.

Over a period of two years a study has been made of forty-four boys whose ages varied between 10 to 17 and who lived in a boarding school for dependent boys. The specific problems considered were: 1. Does enuresis disappear with adolescence? 2. If so, how does this occur? 3. What light does the study throw on the treatment of enuresis in childhood? In addition to securing a careful personal and social history, each child was given a complete physical examination, with Stanford-Binet tests and sometimes tests for special abilities, and the personality was studied by a psychiatrist at the Institute for Juvenile Research.

Investigation of the families of the boys revealed that all but seven came from homes that had been broken up by the death of one or both parents or by separation of the parents; twenty came from dependent families; in ten there was a history of mental disease and in six of tuberculosis. In six of the families, there were other persons subject to enuresis.

Sixty-four per cent of the boys presented behavior difficulties other than the enuresis — stealing, lying, truancy and incorrigibility. There was a school retardation of one year in nine cases and of two or more years in thirteen cases; twenty-two boys were up to grade.

The onset of the enuresis dated from infancy in 37 per cent, from the preschool period in 9, from the preadolescent period in 2 and from adolescence in 2 per cent. The date of onset was not learned in 50 per cent. Fourteen per cent of the boys were overweight, 32 per cent were up to weight and 54 per cent were underweight. Sixty-four per cent were of vagotonic make-up, 13 per cent sympathicotonic and 23 per cent not classified.

The intelligence quotients were below 70 in 7 per cent, from 70 to 79 in 25 per cent, from 80 to 89 in 30, from 90 to 109 in 36, and from 110 to 119 in 2 per cent. Phimosis was present in 8 per cent, and 30 per cent had been circumcised. Conditions of the lung suggestive of tuberculosis were present in six boys. Urinalysis showed albuminuria in one boy. The blood Wassermann reaction was uniformly negative.

Sixty-six per cent of the boys showed psychoneurotic features such as restlessness, complaints of nervousness, tics, stammering and other difficulties of speech, phobias, anxieties and sleeplessness. Eighteen per cent presented resistiveness, negativism or outbursts of temper. Onanism was acknowledged in 80 per cent, denied in 4 per cent and not learned in 16 per cent. The boys expressed dissatisfaction with facts of the surroundings as follows: with the military regimen and employees, 27 per cent; with the demands of the school, 18; with associates, 16; separation from home, 18; with living conditions, food, etc., 8; with work demands, 13; with being unsuited for the school, 8; miscellaneous, 8. Only 6 per cent did not express dissatisfaction. Sixty-four per cent expressed shame concerning the enuresis, and 36 per cent were indifferent.

The attitude of schoolmates and personnel toward the enuretic boys was uniformly one of disapproval and sometimes of intolerance, many of the boys using such terms as "skunk," "midnight sailor" and "polecat" to describe their attitude. The enuretic boys were segregated in a special dormitory in each cottage and were punished by deprivation of privileges and sometimes corporally. It was a regular practice to limit the amount of liquid and food taken at the evening meal.

For the purposes of this study, all these means of discipline and treatment were discontinued. Instead, the habit and the personality characteristics

and the significance of masturbation were discussed frankly with each boy in private. Each was encouraged to feel that he would succeed in controlling the habit. Any special interests a boy might have were fostered in every way. Group encouragement was also given with rewards for continence, a gold star on his card for each dry night and charts showing progress in the different cottages. The greatest emphasis was laid on the need for the boy to assume the responsibility for his own treatment. Many of them adopted self-imposed modes of treatment, which included: limitation of fluid intake; limitation of the amount of food at the evening meal; limitation of certain types of foods such as tea, spicy and sour food, lean meat; cessation of evening recreational activities, such as running and excited playing; bitters and special capsules obtained from parents; religious reading; purchase of an alarm clock, and awakening themselves at night without special aid. Many of the boys said that each night on retiring they would plan to wake in order to void urine; at first sometimes as often as five or six times in the night. When persisted in, these plans of self-imposed treatment resulted in definite improvement and ultimate cure.

The results of treatment were: 27 per cent cured, 25 per cent improved and 48 per cent as yet unimproved.

The conclusions reached are: 1. Enuresis, except when of organic origin, disappears during adolescence. 2. Enuresis in adolescent boys is closely related with psychoneurosis and vagotonia. 3. Cessation of enuresis in the adolescent occurs gradually and depends on a desire to be socially acceptable with assumption of personal responsibility. 4. A plan of treatment for enuresis in younger children should include giving them an understanding of self-reliance and a desire for social acceptance.

DISCUSSION

Dr. Ralph C. Hamill: This subject is of importance to any one interested in the adult psychoneurotic problem, especially along the line emphasized in the paper — the assumption of responsibility by the person for his performance. When one thinks of what goes on in sleep, the relationship of what we call conscious and unconscious states, the idea that the psychoneuroses are the result of the action of the subconscious as against the conscious, then we have in children a distinct entity that bears directly on this subject; getting the child to assume responsibility for itself in sleep seems to me to be a step in the right direction, as against all such efforts at medical care of this condition: suggestion, limitation of fluids or any other of the well known methods of treatment. After all, they may save the mother the trouble of washing the sheets and save the mattress, but they do not do much to save the child. It is a move in the right direction so far as the assumption of responsibility by the child is concerned, the "cure" being secured as something coming from the outside rather than the inside. I was interested in what Dr. Schroeder said about the assumption of responsibility of the child in awakening himself. Recently I have had a distressing case in a man who has greatly desired continuous sleep during the night, but because of a habit established in childhood because of enuresis, he has been unable to have this continued sleep; at the age of 50, the mistakes of the child are taking their toll.

The relationship to onanism is interesting, and I think the relation of bed-wetting and dreams could be well taken into consideration. What percentage are of the fear nature, what percentage are those of being in the toilet, and in what percentage is the impulse to follow this out carried through? That has been a form of dream I have never failed to obtain from children 8 or 9 years of age. The children have had fear dreams and the relationship of fear to neurosis seems to me an interesting side of the question. Every one realizes the relationship of the desire to empty the bladder and fear; in these dreams there seems to be some such relationship.

Dr. Meyer Solomon: We have heard much recently about the psychologic side of enuresis, especially that it expresses a wish on the part of the person

to get away from a given situation to gain pleasure. What we have heard does not seem to back this up, and I have had no case that does. On the other hand, the average child with enuresis is either ashamed or indifferent. I believe that in these instances we have an overirritable nervous control of the bladder and any factor, such as insufficient rest, malnutrition and excitement that leads to a certain degree of instability will produce the enuresis. In the effort to control it, as brought our in the paper, the child must be on guard more, take less water if he finds that taking much water at bedtime causes enuresis, he must be awakened a couple of hours or more after falling asleep and must use more personal effort to control the habit. As I see the situation, there is a definite nervous instability by virtue of which the control of the bladder is lessened and the efforts on the part of the patient are intensive to overcome that defect. Although the psychologic aspects are to be considered, there is no evidence that enuresis expresses a wish of any sort on the part of the child, whether to get more attention from the parents or otherwise. If the psychologic method is adopted, one is apt to go wrong in most cases, while better results are to be obtained by handling the condition from the other angle.

DR. HERMAN M. ADLER: The psychologic aspect of enuresis is particularly interesting to us at the Institute because it is a military school that takes very young boys. Problems of this kind make children unpleasant at home and offer the parents a common excuse for sending them to a military school. The experience during the war was that these cases were not worth the time they took, and the boys were almost invariably summarily discharged from the army. The enuresis was almost without exception a recurrence of a habit of childhood, and the military discipline would have no effect on it. It was the older men who usually did best under military training, and the young recruits who volunteered and were below the draft age did not do nearly so well. The observation was that military life for boys under 19 was not valuable.

Another consideration is that while the points Professor Boder has mentioned are important and should be looked into, the fact remains that even at this military school enuresis is the exception as it is elsewhere. Dr. Schroeder has shown that enuresis may be the result of other than organic causes. This has been dealt with by many. Dr. Schroeder mentioned hypnotism. Dr. Finkelstein said they cured all cases by hypnotism in his clinic.

The experience in this type of study in the army and in institutions shows that enuresis seems to be one of the signs of constitutional inferiority. These patients are recognized as inferior persons who do not adapt themselves to the community, but as persons who maintain an infantile reaction. The child does not get over it automatically because of the development of his nervous system and control, and when he finds the social aspects of it, it must be considered there is a psychologic reaction or failure to react to the social situation. In other cases whether it is a constitutional incapacity that does not automatically develop the control, or whether it is the social reaction, it is a problem of inhibition. Whether one calls it a "wish" or discomfort from a full bladder, this person is so constituted that he does not inhibit an impulse of this sort for the sake of benefit, and that is what characterized the psychopath in other ways. He fails to inhibit the impulse for the sake of reward. If this is a pathologic condition, it probably is a deep-seated type, and military training will not meet the condition. One must either remove the patient from the environment, which is done by individual work, or in some other manner give a chance for such control to be developed.

DR. ALFRED P. SOLOMON: Was there a tendency for the habit to run in other members of the family in any of your cases? I am reminded of a patient, aged 17, who was admitted to Cook County Hospital because of an acute infection and who, on routine examination, was found to be suffering from enuresis. It was learned that four brothers had suffered from the same

condition; three sisters were spared. When I questioned the mother about this she regarded the matter with little concern, saying that the patient would soon get over this as had his four brothers, three of whom lost the habit while members of the American Expeditionary Forces, and the fourth not until he married. A thorough examination was made to rule out physical defects, and it was decided that the enuresis was due to the family tendency, this in turn probably being due to the mother's blunt acceptance of the situation.

DR. SCHROEDER: The point Dr. Hamill brought out regarding the relationship of dreams and enuresis is interesting. Most of the patients had dreams, but I was unable to bring out anything of special significance. Many of them said they did not dream. The habit of awakening at night in the children is not proportionate to the enuresis, and does not continue when bed-wetting ceases. I doubt whether this is the explanation in the case of the man he mentioned.

Dr. Meyer Solomon does not believe this is a protest. I did not wish to give that impression, but wished to show that the children assumed responsibility only when they realized that we had stopped trying to cure them and that if they wished to stop the bed-wetting, they must do it themselves. It was interesting to note that they picked out as treatment the methods that they seemed to have noticed for themselves would cure.

Professor Boder brought up the question as to why neurotic children seem to be more willing to lie in a wet bed than other children. It is hard to answer that, for children who are not bed-wetters do not have wet beds. It was not my experience that children enjoy lying in the wet bed. In some instances in which the children complained that it was too cold at night, arrangements were made so that they had a bathrobe and slippers that were warm, in order to overcome their unwillingness to expose themselves to the cold. There seemed to be a larger amount of enuresis in the winter, but the series is so small that I did not consider that significant. Children often said it was too far to go to the toilet, and that they did not like to go, but I looked on that as an excuse for the bed-wetting.

I have nothing to offer in connection with increase in the size of the bladder. Some work is being done on this question by Amberg at present, but there is not much light on its relation to enuresis so far.

As to the question raised by Dr. Alfred Solomon regarding the incidence of enuresis in other members of the family, six of these forty-four patients gave a history of enuresis in other members of the family, but I had no such striking examples as the one he mentioned.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, April 21, 1927

HENRY R. VIETS, M.D., *President, in the Chair*

PINEAL SYNDROME. Presented by DR. GILBERT HORRAX.

Although there is evidence in the embryo that the pineal gland has glandular structure, studies of the organ in postnatal life do not reveal any evidence of glandular activity. Experimental studies have indicated that extirpation of the pineal gland may be associated with a condition of hastened maturity (Foa, Horrax), but, on the other hand, the studies of Dandy and others on extirpation have given entirely negative results. The best evidence, therefore, comes from careful clinical and pathologic studies of tumors of the pineal gland in human beings. With this fact in mind, the following cases are reported.

CASE 1.—A boy, aged 9, was admitted to Peter Bent Brigham Hospital on Aug. 20, 1925. The family and past histories were unimportant. Headaches,

vomiting and double vision had been present for six weeks. A staggering gait, progressing to inability to walk, had been present for three weeks. Examination showed: slightly enlarged external genitalia for the age of the patient, bilateral choked disks, loss of conjugate movements of the eyeballs upward and marked hypotonia of the extremities. The pineal region was exposed by operation on September 9, but the child died before twenty-four hours had passed. Necropsy revealed a large tumor of the pineal body, which was pathologically a teratoma. The testes showed a microscopic picture comparable to that seen at the age of 15. The other glands of internal secretion were normal.

CASE 2.—A man, aged 40, was admitted to Peter Bent Brigham Hospital on Nov. 17, 1925. The family and past histories were without significance. Pressure symptoms with marked failure of vision had been present for fifteen months previous to admission. Staggering and drowsiness had been present for four months with the onset recently of dysphagia and dysarthria. Examination revealed: bilateral choked disks, pupils which did not react to light although some vision remained, loss of upward and downward conjugate movements of the eyeballs, bilateral clonus and the Babinski sign. A subtemporal decompression was performed, but death occurred after three days. Necropsy revealed a small tumor replacing the pineal body. There was not any evidence that pineal tissue had ever existed. The pathologic diagnosis was ganglioneuroma.

CASE 3.—A boy, aged 7, was admitted to Peter Bent Brigham Hospital on June 1, 1926. At the age of 3 he had developed pubic and axillary hair of adult type, the external genitalia reaching adult proportions at the same age. The voice changed to the adult masculine type at this time also. A squint of the right eye had been present for one year. Polyuria had existed for one month and diplopia for two weeks. Examination showed the boy to be markedly oversized with fully developed adult pubic and axillary hair and external genitalia. He had bilateral choked disks of 5 diopters and a weakness of the right abducens muscle. Operation disclosed a tumor in the region of the third ventricle, but the child died shortly after a partial extirpation of this growth. Necropsy revealed a large tumor of the third ventricle, a normal pineal body and normal glands of internal secretion other than the testes. These showed a microscopic picture in every way compatible with those of an adult. Pathologically the tumor of the third ventricle was a ganglioneuroma.

THE PSYCHOLOGY OF CONDUCT ACCORDING TO PIERRE JANET. Presented by DR. PERCIVAL BAILEY.

In the lectures delivered at the Collège de France, in the winter of 1925 to 1926, Pierre Janet developed a summary of his psychologic theory, especially concerning the hierarchy of conduct and the different types of persons corresponding to the various levels of conduct. This hierarchy may be summarized in the following table:

Functions or Tendencies

Superior	Progressive	Man of genius
	Experimental	Practical man
	Rational	Systematic man
Intermediate ..	Reflective	Egoistic-logical man
	Assertive	Prelogical man (moron)
	Intellectual	Primitive man (imbecile)
Inferior	Social	Social animals (social idiot)
	Perceptive	Lower animals (last degrees of idiocy)
	Reflex	

The table is arranged so that the more complicated conducts and those which have arisen later in evolutionary development are above. The superior tendencies suppress and inhibit the lower ones, a mechanism anthropomorphized by Freud in his conception of the censor. Janet accounts for the neuroses by different degrees of activation of these tendencies or mechanisms, this being the origin of his theory of psychologic force and tension.

TRIGEMINAL NEURALGIA AND OTHER FACIAL PAINS. Presented by DR. I. OLJENICK.

A number of arguments tend to show that a primary location of trigeminal neuralgia lies in the peripheral division; there are others, however, which may equally be used to prove that the gasserian ganglion may be considered as the seat of this type of neuralgia. Among the last the most important argument may be found in the microscopic anatomy of the semilunar ganglion, as investigated by Frazier and Whitehead, who proved that the cell group of each division has its separate place within the ganglion, while ontogenetically the ophthalmic portion is differentiated at an earlier period than the maxillary and mandibular cell groups as are also its central as well as its peripheral processes. Van Valkenburg has found that in lower vertebrates the ophthalmic portion remains separate from the combined two other parts. Thus, a disturbance of part of the ganglion may give rise to a one division neuralgia or a neuralgia of two branches.

There are many arguments in favor of the peripheral view. One of these deals with the favorable results obtained by peripherally applied therapeutic agents, especially chemically pure trichlorethylene, obtained by substituting hydrogen atoms in ethylene, which may also act as a narcotic if taken in large doses. In small doses, from 20 to 25 drops inhaled three times a day, it has been proved to be without noxious effects on internal organs or metabolism. It shows an elective effect on the hypersensitive trigeminal nerve. The results obtained in the Out-Door Department of the Neurological Clinic of the University Hospital in Amsterdam are encouraging.

Other facial pains may be confounded with trigeminal neuralgia: (1) a condition which I consider as vascular spasm pains, occurring nearly always in elderly people and involving the whole side of the face from the very onset with longer lasting attacks. Sensory root section is useless in this condition. Perivascular sympathectomy of the carotid artery and dissection of the cervical sympathetic cord have been tried. (2) Glossopharyngeal neuralgia and Sluder's syndrome of the sphenopalatine ganglion are important in the differential diagnosis of the facial pains.

My conclusions are: 1. It has not been proved that the gasserian ganglion is the only location of the lesion of trigeminal neuralgia. The results of the various treatments can more readily be explained by acceptance of the view that trigeminal neuralgia, generally, is a disturbance of the peripheral branches, gradually advancing to and into the ganglion. 2. As the pain is only rarely uninfluenced by trichlorethylene, it should be tried in every case of trigeminal neuralgia. 3. In the diagnosis of facial pains occurring without apparent cause, distinction should be made between trigeminal neuralgia, glossopharyngeal neuralgia and vascular pains, for which the name prosopalgia might be used, and eventually also sphenopalatine neuralgia.

DISCUSSION

DR. W. J. MIXTER: We have not used trichlorethylene. I am much interested in Dr. Oljenick's use of it. I was also interested in his presentation of the forms of neuralgia occurring in the face, and the various suggestions concerning the causes of neuralgia, or, rather, its psychic origin. In a certain number of cases, the patients are operated on without relief.

DR. STANLEY COBB: I have used trichlorethylene in one difficult case with complete success. I believe it is well worth using, previous to operation. Dr. Oljenick has made a distinct advance in the treatment of patients with this extremely troublesome disease.

Book Reviews

GESUNDHEIT UND KRANKHEIT IN NIETZSCHE'S LEBEN UND WERK. (Abhandlungen aus der Neurologie, Psychiatrie, Psychologie und Ihren Grenzgebieten, Heft 38). By Dr. med. et phil. Kurt Hildebrandt, Oberarzt an den Heilstätten Wittenau bei Berlin. Price, M. 8.40. Pp. 160. Berlin: S. Karger, 1926.

This monograph is an expansion of the author's earlier study of the beginning of Nietzsche's psychosis, restated in the form of an intensive discussion of the facts in Nietzsche's life and writings. It is intended to counteract the journalistic account of Nordau and the evidently rather "ununderstanding" presentation in Moebius' pathography. With the recent widely accessible account of Nietzsche's personality and work published in Will Durant's "Story of Philosophy," and this monograph, the American reader could not help being stimulated to go to the actual writings of this extraordinarily outstanding and provocative figure of the end of the nineteenth century. Hildebrandt aims to humanize the entire development and to dispel the offhand classifications which formulate the facts baldly as constituting degeneracy, decadence and general paralysis, and although he does not want to shake the claim of general paralysis too emphatically, he offers a picture and a discussion that appeal strongly to any one accustomed to a genetic-dynamic conception of man and his diseases.

It appears that the only full record of hospital observation (after the final collapse in January, 1889, led to Nietzsche's admission to the Jena Psychiatric Clinic from Jan. 18, 1889, to March 24, 1890) is lost. What Moebius copied from the original record still accessible to him, and the utterances of Binswanger (who claimed that there was general paralysis without syphilis in 70 per cent of the cases), Ziehen (atypical general paralysis) and Vulpius (recurrent iritis of the left eye) should today be read with the definite realization that no conclusive and adequately controlled facts are available. The early nineties was the time when the diagnosis of general paralysis was probably made altogether too often (in Kraepelin's clinic probably over 100 per cent too often). To look for the cause of general paralysis in Nietzsche's short service as ambulance helper during the war of 1870-1871, ending with diphtheria and protracted dysentery, may in the end be as unnecessary as it would be non-satisfying. The entry in the Jena record ("syphilitic infection, 1866, according to Overbeck's statement") cannot now be verified; but it appears that the corresponding note in the brief Basel record consists only of a reply to a leading question about infection, reading — "yes, twice, 1866" — a reply given in a confused period and probably referring to the fear of cholera infection in 1866. The quest for the characteristic writing defects (tremor, etc.) of general paralysis does not yield any positive evidence. The disturbance of memory as far as it seemed to exist, shows only for the events following the crisis of 1889 and does not seem characteristic for general paralysis. Nietzsche's signing himself as "Dionysos," as "the Crucified," during the expansive phase of the psychotic episode is not a highly megalomanic flight for the prophet of the Superman. His collapse in the street and inability to get up, the difficulty his landlord had to lead him to his room, then the two days of "lethargy" followed by a confused excitement, with rapid shifting of topics and activities, with fleeting identifications, and the later statements of "hallucinations" (not especially frequent in general paralysis) leave one much in doubt.

Evidently the return of greater coherence in reminiscing, and again the tendency to brood and to produce confused soliloquies, and the rest of the meager facts between 1890 and 1900 could hardly be used for decisive diagnostic purposes. General paralysis and catatonia (in the wide sense in which the latter term was used by Kraepelin) were the diagnoses discussed in the nineties as remembered by the reviewer.

Hildebrandt discusses the relation of the symptoms to Kretschmer's concepts of constitution, but without becoming decisive. Autopsy was not performed.

The case of Nietzsche may never be cleared up. Hildebrandt has at least broken down much of Moebius' peremptory and in part "ununderstanding" verdict and the theory that general paralysis existed in the Zarathustra period. As a contribution to the discussion of the justification of inferences of decadence and degeneracy, and to the discussion of the relation of the man and the disease, the monograph is stimulating. It has definitely stirred the reviewer to a sympathetic rereading, and partly first reading, of many parts of Nietzsche's work too often judged only from quotations. The line between normality and abnormality is difficult to draw. Yet it looks as if far more of Nietzsche's work were the product of Nietzsche's "normality" than of his "disease"; Hildebrandt depicts Nietzsche's susceptibility to the rôle of a prophet of his idol Dionysos versus Apollo and Plato and of his living idols, Schopenhauer and Wagner, his unusually early appointment to the professorship in Basel (at 24, before he had attained his doctorate in philology), his enthusiasm for both Cosima and Richard Wagner, his disappointment in Wagner's swinging toward Catholic medievalism in "Parsifal" and Wagner's need of display at Bayreuth, the drudgery of the professorship (combined with teaching at the gymnasium), the characteristics of the aggravation of the "sick headaches" (migraine and vomiting) and depression-like invalidism that led to retirement on a pension in 1880; then the rebound connected with his intoxication with the Zarathustra message (1881-1884); then the urge to reach a public in prose and in a more systematic philosophy if it could not be reached in poetical rendering —all these phases are described with a great deal of inner consistency and freedom from the decadence and degeneracy notions of the nineties and the implications of general paralysis. Hildebrandt's picture and argument go a long way to make one suspect more consistency with a psychodynamic crash due to circumstances. He does not dispose of the diagnosis of general paralysis, but he leaves the reviewer decidedly with the impression that the lack of an autopsy is a tragedy. It might easily have shown an absence of general paralysis and made more probable a constitutional psychodynamic development. Degeneracy and decadence might be too easy a way of disposing of the concrete situations and their cumulative effects. However that be, the concepts mean little to us today as compared to the more concrete and specific call for an understanding of the life of the patient; the fate of a prophetically inclined minister's son, enthusiastic over his conception of pre-Socratic thought and dionysian ideals, disappointed in his hero-worship of Wagner, but to the last in conflict with his idol, and wrestling with his transvaluation of values and his vision of Zarathustra and a spiritualized conception of the philosophy of evolution (with an eternal recurrence of the same cycles) as opposed to the relapse into medieval cult.

INTRODUCTION A L'ÉTUDE DE LA PSYCHOGÉNÈSE. By MAURICE DIDE. Price, 12 francs. Paper. Pp. 221. Paris: Masson et Cie, 1926.

This little book most assuredly lives up to its subtitle: An Essay on Evolutive Biopsychology. In this sense it gives really eloquent testimony of the author's brilliancy in the best tradition of the French school. At times, of

course, its highly spirited style makes it somewhat difficult to read; the "élan psychogénètique," to which the third chapter is devoted, has carried the author to heights almost too elevated to follow. But that is perhaps the advantage of the book; it startles the reader, stimulates reactions of various kinds and is never tiresome. Some of the conceptions are astonishingly keen and daring, whereas others date back to our forefathers. The whole work is inspired by a life-asserting optimism and a positive philosophy.

The book is difficult to summarize, but its principal thoughts may be formulated as follows: Radiant and convergent energy are the two fundamental tendencies of both the inorganic and the living world. They are encountered in the atom, and through progressive evolution they reach their culmination "in the moment of psychologic liberation." The doctrine that function creates the organ is generalized by the author into the statement: energy creates the molecule and the molecule, in spite of its stability in its simple forms, eventually undergoes mutations which determine its complexity. In fact, psychologic evolution implies a parallel evolution of the brain, rendered efficient by neurovisceral synergies, which are themselves the product of circulant energy (diastase). There is a definite distinction between the inorganic and the organic: the life processes are not reversible, and the author emphatically rejects the possibility of any reversibility as claimed in certain theories. In the life cycle of the nerve cell, four phases are distinguished: (1) proteogenesis, corresponding to accumulation of energy; (2) chromatolysis, corresponding to experimental fatigue; (3) proteostasis, corresponding to a state of inhibition; (4) proteolysis, corresponding to fatal injury.

Emphasis is put on the close relation that exists between the first two of the phases mentioned and the liver; liver insufficiency deprives the organism of its antitoxic functions, resulting in mental confusion. An interesting definition is given to chromatolysis: precipitation of colloid matter known as flocculation. Much is said about biologic syntheses and their importance, but at times it is difficult to see what this term really means. The definition of instinct, also, does not seem to be particularly clear: "Instinct, the essential energy of life, regulates ontogenetic and phylogenetic evolution and contains virtually all the most differentiated psychologic forms." In instinct, the two fundamental tendencies are contained as follows: convergent energy becomes the instinct of conservation, whereas radiant energy assures the temporal destiny of the individual and becomes the instinct of reproduction.

The chapter on "l'élan psychogénètique" and the emotions is highly interesting. Eppinger and Hess are quoted in regard to the organic substratum of active innervation and inhibition; Spinoza is once more given full credit for the discovery of the biologic roots of consciousness; emotional shock, immunization and emotional anaphylaxis, called biologic realities, and various neurovegetative disturbances are brought into causal relation with constitutional mental diseases, always in reference to radiant and convergent energy.

In the following chapters is sketched an "Aufbau" of the relation between the outside world and mental life, beginning with simple perceptions and terminating with abstract mathematical thinking. Eupraxia, apraxia, aphasia, etc., are dealt with extensively, and almost all the theories in question are mentioned and many new terms introduced. Toward the end, one again meets the two forms of energy: Ideo-affective synthesis is the equivalent of a continuous variation of psychogenetic radiant energy and gnostic and rational convergent energy, pleasure corresponding to a supremacy of the former and pain and distress resulting from preponderance of the latter.

The work is thus, as a whole, largely theoretical, exhibiting certain aspects of medical metaphysics at their worst as well as at their best—for, after all, the book is written in an agreeably stimulating manner. It will be of interest to those who appreciate an orientation of this kind.

There is a biblography of 256 books and articles, for the most part French, although German and American contributions are also represented.

APHASIA AND KINDRED DISORDERS OF SPEECH. By HENRY HEAD, M.D., LL.D., EDIN., F.R.S. Volumes 1 and 2. Price, $20. Pp. 979. New York: The Macmillan Company, 1926.

The understanding of the principles underlying the production of speech and its disorders has always challenged the minds of great neurologists. It is not surprising, therefore, that Henry Head, who has contributed so largely and so well to neurology of the present day, has taken up this subject.

The book is divided into two volumes. In the first part, the discussion of the subject is included. The second volume is devoted to a series of clinical reports of illustrative cases arranged in numerical order. In the introduction to the second book, a summary of these cases is given.

Volume 1 is divided into four parts. The first part is historical. Head has not attempted to give a consecutive and coherent historical sketch and quotes only that work which to him is pertinent. The first chapter is headed "From the Schoolmen to Gall"; the second "Bouillaud and Broca"; the third, and perhaps the most interesting chapter in the whole volume, "The Views of Hughlings Jackson on Aphasia." The fourth chapter is headed "The Diagram Makers," and is divided into the views of the English and the German Schools. The fifth chapter is headed "Marie the Iconoclast" and the sixth "Chaos," under which there are the following headings: (*1*) Henschen and anatomical localization of function; (*2*) Von Monakow and diaschisis; (*3*) Liepman and apraxia; (*4*) imperception or agnosia; (*5*) the word as a unit of thinking and speaking and (*6*) the clinical psychologists. A chapter on the "Historical Retrospect" finishes this first part.

The second part of the first volume presents Head's views on aphasia. After some introductory remarks, the methods of examination are presented with clinical examples; this is followed by a presentation of his views on the nature of the disturbances of function and his classification. In the third part, he discusses what is meant by localization of function and the presentation of the anatomic site of the lesion in some cases of aphasia. The fourth part is divided into a discussion of "vigilance," cerebral localization, language and thinking, and his final conclusions and summary.

It is difficult to review adequately a work of this kind. To do it justice one would have to write a thesis on the subject. The reviewer, however, wishes to comment on certain aspects of the problem. Two fundamental and different points of view on aphasia have been held and defended for many years. In the first group are included persons who favor extreme localization and the diagram makers, to whom speech is the result of the combined activity of various parts of the brain, disturbance of which causes disorders of speech, according to the location of the lesion. This view was largely held until Marie threw a bomb into the accepted theories and attempted to show that extreme localization is impossible. It is interesting that perhaps the clearest views on aphasia which have ever been held are those of the great English philosopher Hughlings Jackson, and yet they were lost sight of for many years even by the British; Pick, a German, was the first to appreciate and to call the attention of neurologists to Jackson's neglected theories.

Head's conclusions regarding the nature of disorders of speech is based on the clinical study of certain war material. His localization is necessarily only approximate, but his clinical studies are excellent. He has accepted most of the views of Jackson, but has made new grammatical classifications which he terms the verbal, syntactical, nominal and semantic defects. Boiled down, they are merely elaborations of the old motor and sensory aphasia, with the old localization.

It is a question whether the classification that Head has made can stand the test of experience. A fundamental error lies in the fact that his tests were not checked up on normal persons; at least, there is no mention of it. The reviewer questions whether any series of tests can ever adequately evaluate in all patients a standard method of measuring disturbances of speech.

However, Head has done a splendid piece of work. It is hardly necessary to say that he has contributed greatly to the knowledge of speech and its disorders. Every neurologist should read the book, particularly the chapters on localization and its interpretation, vigilance, language and thinking. Throughout he refers to his sensory studies, and it would be well if the student were to read his papers on this subject prior to the perusal of these volumes. This study is one of the great contributions of the time and ranks with the work of Broca, Jackson and Marie. There is no greater praise.

READINGS IN ABNORMAL PSYCHOLOGY AND MENTAL HYGIENE. By W. S. TAYLOR. Price, $4.00. Pp. 789. New York: D. Appleton & Company, 1926.

The editor of this volume has selected excerpts from about 227 papers on various topics of abnormal psychology, and has organized them into twenty-six chapters. The title of the book is somewhat misleading in that only one paper is devoted to the large subject of mental hygiene. It seems hardly justifiable to devote one half of the title of such a large volume on the basis of this one paper. The purpose of the book is to provide the student with a source book in the rapidly growing and widening field of abnormal psychology. The method of selecting parts of a large series of papers was chosen to give a more elastic presentation of a broad subject — to give a glimpse at the literature and the views of different authors on similar subjects.

Jastrow, in an interesting introduction to the volume, discusses the changing points of view in this field during recent years. He shows the changes which were necessary for the philosophically minded conventional psychologist to develop an interest in, and an understanding of, the abnormal. "They had to learn to think biologically, neurologically, behavioristically before they were ready for the reconstruction of their science which brings the abnormal into the focus of their interest." This has been accomplished largely through the technical development of the experimental method and has resulted in the psychologist looking on "mental life as a growth and a direction," and has given him a genetic point of view.

It would be impossible to review the subject matter of a book of this type. Its usefulness will vary with the needs of the student. As a source book for students wanting references and a point of view on certain aspects of the subject, the book will no doubt prove of value. It can give no more than a superficial glimpse at the subject and will therefore be of less use to the student requiring a more connected and detailed statement of the various topics. The editor utilizes freely the clinical methods of presentation. A great many of the excerpts deal with case material, frequently given without any of the interpretative parts of the paper.

INTRACRANIAL TUMORS AND SOME ERRORS IN THEIR DIAGNOSIS. By SIR JAMES PURVES-STEWART. Pp. 195. London: Humphrey Milford, Oxford University Press, 1927.

It is rarely that any physician, even a psychoanalyst, makes his confession in public, yet this is what a modest neurologist has done. Purves-Stewart reports 121 verified cases of tumor of the brain, and he not only gives his good results but emphasizes his mistakes.

The grouping of his cases is the usual one. In discussing the signs common in intracranial tumors in general, he mentions paroxysms of yawning or hiccup which may be produced especially by tumors of the posterior fossa. In tumors of the prefrontal lobe, he comments on the fact that the mental symptoms resulting from such lesions are not characteristic. The occasional occurrence of unilateral nerve deafness in tumors of the frontal lobe is probably

the result of pressure. Purves-Stewart's experience with tumors of the parietal, occipital and temporal lobes is that of most neurologists. The same thing can be said about cerebellar tumors and the rarer lesions found throughout the brain. The most interesting parts of the book, however, are the three last chapters, which are headed: Gross Errors in the Diagnosis of Cerebral Tumors, Some Pitfalls in Diagnosis, and Errors — Avoidable and Unavoidable. It would contribute largely to the knowledge of focal diagnosis if all experienced neurologists were to follow the example of the author. They would perhaps find that their percentage of errors would at least equal that of the author.

The conclusion that one can reach from reading this refreshing book is that the most pertinent problem in neurology today is the proper diagnosis of intracranial lesions.

HIRNPATHOLOGISCHE BEITRÄGE. By DR. KARL SCHAFFER. Pp. 315. Budapest VIII. Balassa-U, 1927.

This is the sixth volume of reprints from Professor Schaffer's Neuropsychiatric Institute in the University of Budapest and contains reprints of work that has been turned out by him and by others under his direction.

The work is of high order and reflects great credit on Professor Schaffer's industry and scientific ability.

DER BARANYSCHE ZEIGEVERSUCH. SEINE PHYSIOLOGISCHEN GRUNDLAGEN UND KLINISCHE METHODIK. By ERNST WODAK, M.D., PRAG. Price, paper, 3 marks. Pp. 79, with 26 illustrations. Berlin and Vienna: Urban and Schwarzenberg, 1927.

The author, who has worked with M. H. Fischer in Tschermak's physiologic institute at Prag, presents a review of the physiologic foundations of the much discussed pointing test, with results of experimental work of his own. Pathologic variations in the test are not considered. The conflicting results reported by various observers find much ground for explanations in the great complexity of the factors concerned in the test. The material is admirably arranged and clearly presented; the book will be heartily welcomed as it fills a long felt gap in the literature on the subject. After a brief introductory chapter on the general foundations of the test, the material is dealt with under the heads of: nonlabyrinthine influences — muscular, sensory, position of head and eyes, spontaneous symmetrical deviations, etc.; factors that influence the results through stimulation of the labyrinths; general considerations in the analysis of the test; results of personal experiments with rotation and ear douching; awareness of deviations and their correction, and summary. Following this the literature, almost entirely German, is reviewed and the clinical applications of the test are described. A last chapter deals briefly with related tests.

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